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The Relationship between the Triglyceride-Glucose Index and Vitamin D Levels in American Adults

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Abstract: The triglyceride-glucose (TyG) index is a cost-effective, reliable and validated measure of insulin resistance. Furthermore it is a promising biomarker of Metabolic Syndrome (MetS), Type-2 Diabetes (T2DM) and premature atherosclerotic cardiovascular diseases (ASCVD). Although groups from numerous countries especially Asia have shown an inverse relationship between Vitamin D levels and the TyG index, there is a severe paucity of data by US investigators. Accordingly, in the present preliminary report we investigated the relationship between tertiles of TyG index and Vitamin D levels and also undertook correlations with relevant variables. The TyG index increased significantly over tertiles in the combined group of MetS (n = 41) and controls (n = 37). However there was no significant change in plasma Vitamin D levels over tertiles, p = 0.15. We show a modest but significant correlation between TyG and Vitamin D. In conclusion in this pilot study we failed to see a significant decrease in Vitamin D levels over increasing tertiles of the TyG index but showed a modest inverse correlation. Hence future studies with much larger sample sizes of American participants can settle this important issue.

Keywords: triglycerides; glucose; vitamin D; insulin resistance

1. Introduction

The triglyceride-glucose (TyG) index, is a cost-effective, reliable and validated measure of insulin resistance [1,2]. Furthermore the TyG index has been shown to be a promising biomarker of cardio-metabolic disorders including Metabolic Syndrome (MetS), Type-2 Diabetes (T2DM) and premature atherosclerotic cardiovascular diseases (ASCVD) [1,2]. Also in numerous studies it has been shown to be superior to homeostasis model assessment insulin resistance (HOMA-IR) [1,2].

We recently reported in a general US population using the National Health and Nutrition Examination Study (NHANES) and showed in 5380 Individuals aged 20–80 years that the TyG index, in this cross sectional study, was superior to HOMA-IR in predicting prevalent MetS in this representative US adult population [3]. However there is sparse data from American investigators examining the utility of the TyG index.

Previously we have shown in North American Adults that Vitamin D levels are significantly lower in patients with MetS without the confounding of smoking, T2DM, ASCVD and macro-inflammation [4]. This decrease in levels could not be explained by adiposity, sun exposure, renal disease and abnormalities in mineral metabolism. Vitamin D levels correlated with fasting glucose and HOMA-IR in the MetS patients. Although investigators from numerous countries especially Asia have shown an inverse relationship between Vitamin D levels and the TyG index [5–7] there is very scarce data by US investigators. Accordingly, in the present communication we

investigated the relationship between tertiles of TyG index and Vitamin D levels and also undertook correlations with relevant variables.

2. Patients and Methods

Both controls and MetS participants aged 21–72 years were recruited from Sacramento County, CA using the criteria of the Adult Treatment Panel III (ATP III) as detailed previously [8]. Participants were defined as having MetS, if they had at least three cardio-metabolic features of MetS: increased waist circumference (≥40 inches for men and ≥35 inches for women, elevated triglycerides (≥150 mg/dL), low HDL-cholesterol levels (<40 mg/dL for men and <50 mg/dL for women), high blood pressure (systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mm Hg) and high glucose level (≥100 mg/dL). Important exclusion criteria for all subjects included diabetes defined by fasting blood glucose level >125 mg/dL and HbA1C > 6.4%, clinical ASCVD, acute or chronic inflammatory disorders, and history of smoking and lipid lowering therapy. None of the volunteers were taking vitamin supplements including Vitamin D. Additionally, all participants in the study had a high-sensitive C-reactive protein (hsCRP) level <10.0 mg/L and a normal white cell count. The study was approved by the institutional review board at the University of California, Davis and informed consent was obtained from all participants.

Plasma lipids, lipoprotein profiles, and glucose were assayed by standard laboratory techniques in the Clinical Pathology Laboratory as described previously [8]. Insulin levels were assayed by ELISA (Linco Biosystems, St. Charles, MO, USA) and homeostasis model assessment insulin resistance index (HOMA-IR) was calculated from glucose and insulin levels as described previously [3]. Total Vitamin D (25-hydroxy-vitaminD) levels (both D2 and D3) were quantified by LIAISON immunoassay as reported previously [4].

The triglyceride-glucose (TyG) index was calculated as reported previously [3]:

Ln [fasting triglycerides (mg/dL) × fasting plasma glucose (mg/dL) / 2].

Statistical Analysis

SAS version 9.4 (SAS Institute, Cary, NC, USA) was used for statistical analysis and significance was defined as a two-sided p-value < 0.05. Results are expressed as median and interquartile range. Trend analysis of TyG index tertiles in our combined MetS and control participants was evaluated using the Jonckheere-Terpstra (J-T) test for trend. Combining the control and MetS groups, Spearman rank correlation coefficients were also determined to assess the association between TyG index and relevant variables.

3. Results

Table 1 shows the salient characteristics in the combined group of MetS (n = 41) and controls (n = 37). As expected the TyG index increased significantly over tertiles. Whilst there was no gender differences over tertiles there was significant enrichment of patients with MetS with increasing tertiles from 8% in tertile 1 to 88% in tertile 3. Also age, waist circumference (WC), both systolic and diastolic BP, plasma glucose, triglycerides, non-HDL-C, and HOMA-IR increased significantly with increasing tertiles of TyG index. There was no significant increase in hsCRP levels. HDL-C levels decreased with increasing tertiles. However there was no significant change in plasma Vitamin D levels over tertiles, p = 0.15.

We also undertook correlations between relevant variables as depicted in Table 2. There was a significant negative correlation between TyG index and Vitamin D levels. Also Vitamin D levels correlated significantly with plasma glucose and but not with WC, triglycerides, CRP and HOMA-IR. As previously reported there was a significant correlation between TyG index and HOMA-IR; r = 0.51, p < 0.0001 [3].

Table 1. Vitamin D and Cardio-metabolic features across tertiles of TyG Index.

Variable	Tertile 1	Tertile 2	Tertile 3	*p*-Value *
	N = 26	*N* = 26	*N* = 26	
Female/Male, *n*	22/4	20/6	19/7	
(%)	(85/15)	(77/23)	(73/27)	0.31
Control/MetS, *n*	24/2	10/16	3/23	
(%)	(92/8)	(38/62)	(12/88)	<0.0001
TyG-index	7.89 (7.69–8.15)	8.51 (8.4–8.62)	9.11 (8.92–9.34)	<0.0001
25 (OH) Vit D (ng/mL)	28 (23–33)	24 (19–30)	26 (20–29)	0.15
Age (years)	47 (40–59)	53 (48–61)	55 (50–61)	0.03
Systolic BP (mmHg)	120 (105–132)	131 (115–139)	129 (122–136)	0.007

Table 1. *Cont.*

Variable	Tertile 1	Tertile 2	Tertile 3	*p*-Value *
Diastolic BP (mmHg)	71 (65–81)	82 (72–87)	79 (76–86)	0.004
Glucose (mg/dL)	88 (82–92)	93 (90–101)	102 (97–110)	<0.0001
HDL-cholesterol (mg/dL)	57 (43–68)	45 (35–50)	36 (33–42)	<0.0001
Non-HDL cholesterol (mg/dL)	122 (101–149)	151 (134–160)	165 (152–181)	<0.0001
Triglycerides (mg/dL)	63 (51–75)	104 (95–121)	174 (156–208)	<0.0001
hsCRP (mg/L)	1.4 (0.4–4.8)	3 (1.3–5.4)	2.6 (1.7–4.1)	0.11
HOMA-IR	1.7 (0.8–2.3)	2.4 (1.6–3.3)	3.3 (2.4–4.6)	<0.0001

* Jonckheere-Terpstra Test for trend for continuous variables and Cochran-Armitage test for categorical variables. Results are reported as median (25th–75th percentile).

Table 2. Spearman rank correlations (rho) between vitamin D levels and relevant variables.

Variable	rho	*p*
TyG index	−0.25	**0.03**
Age	−0.15	0.18
WC	−0.13	0.27
Blood pressure-systolic	−0.15	0.19
Blood pressure-diastolic	−0.17	0.14
Plasma glucose	−0.34	**0.003**
Plasma HDL-C	0.03	0.79
Plasma non-HDL-C	−0.20	0.08
Plasma triglycerides	−0.21	0.07
hsCRP	0.05	0.65
HOMA-IR	0.06	0.63

4. Discussion

This preliminary report was prompted by the severe paucity of data on the relationship between the TyG index a valid measure of insulin resistance and Vitamin D levels in the American population.

We show a significant increase in cardio-metabolic features over increasing tertiles of the TyG index. However we failed to show a significant decrease in Vitamin D levels as reported in other countries especially from Asia [5–7]. In their systemic review and meta-analysis, Li et al. [5] reported on nine studies: 7 from Asia and one study each from Mexico and Ukraine. They showed a significant association between the TyG index and Vitamin D levels. Whilst we excluded patients with diabetes, 4 of their 9 studies included diabetic patients. Our small sample size per tertile and exclusion of diabetics could explain this discrepancy. These findings in American patients are supported by 2 other studies showing that there was no association with another proxy of insulin resistance HOMA-IR and Vitamin D [9] and small incremental improvement in detecting insulin resistance (HOMA-IR) with Vitamin D in addition to traditional risk factors in non-diabetic adults [10].

We show a modest but significant correlation of −0.25 between TyG and Vitamin D. Also we show a significant inverse correlation between Vitamin D and plasma glucose levels suggesting that with a larger sample size the relationship between TyG index with both Vitamin D and glucose levels could be better appreciated.

In conclusion in this pilot study we failed to see a significant decrease in Vitamin D levels over increasing tertiles of the TyG index but showed a modest inverse correlation. Hence future studies with much larger sample sizes of American participants can settle this important issue since the TyG index in addition to being a validated measure of insulin resistance is fast emerging as an important biomarker of cardio-metabolic disorders including MetS, T2DM and ASCVD [1,2].

Author Contributions

I.J. generated the idea for this publication. B.A.-H. undertook the statistical analyses. Both generated the original version and edited multiple iterations. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

This study was approved by UC Davis IRB: 200715074.

Informed Consent Statement

All volunteers provided written informed consent.

Data Availability Statement

The data is available from the senior author for review on reasonable request.

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Conflicts of Interest

The authors declare no conflict of interest. The Guest Editor who handled this manuscript to avoid any conflict of interest was Prof. Senthil Kumar Venugopal.

Use of AI and AI-assisted Technologies

These were not used by the authors submitting this paper.

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