Triglyceride/Glucose Index (TyG Index) as a marker of glucose status

By Mohammad Zulkarnain

WORD COUNT 4819
TIME SUBMITTED 27-SEP-2021 08:37PM
PAPER ID 77087320

Diabetes & Metabolic Syndrome: Clinical Research & Reviews 15 (2021) 102280

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Triglyceride/Glucose Index (TyG Index) as a marker of glucose status conversion among reproductive-aged women in Jakarta, Indonesia: The Bogor cohort study (2011–2016)

Iche A. Liberty [a, b, **], Nasrin Kodim [b], Ratu A.D. Sartika [c], Indang Trihandini [d], R.M. Suryadi Tjekyan [a], Zulkarnain [a], Masdalina Pane [e], Livy B. Pratisthita [f, g], Dicky L. Tahapary [f, h, *], Pradana Soewondo [f, h]

[a] Department of Public Health and Community Medicine, University of Sriwijaya, Indonesia
[b] Department of Epidemiology, Public Health Faculty, Universitas Indonesia, Depok Indonesia
[c] Department of Public Nutrition, Public Health Faculty Universitas Indonesia, Depok Indonesia
[d] Department of Biostatistics, Public Health Faculty Universitas Indonesia, Depok, Indonesia
[e] National Institute Health Research and Development, Ministry of Health of the Republic of Indonesia, Indonesia
[f] Metabolic, Cardiovascular, and Aging Cluster, The Indonesian Medical Education and Research Institute, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia
[g] Department of Internal Medicine, Universitas Indonesia Hospital, Depok, Indonesia
[h] Division of Endocrinology, Metabolism and Diabetes, Department of Internal Medicine, Dr. Cipto Mangunkusumo National Referral Hospital, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia

ARTICLE INFO

Article history:
Received 25 April 2021
Received in revised form
8 September 2021
Accepted 10 September 2021

Keywords:
TyG index
Glucose
Conversion
Reproductive
Women

ABSTRACT

Background and aims: Reproductive-aged women are prone to type 2 diabetes mellitus. This study aims to evaluate the optimal cut off point of Triglyceride/Glucose Index for predicting glucose status conversion among women of reproductive age.

Methods: This study involved normoglycemic and prediabetes women aged 20–49 years from the Bogor Non-Communicable Diseases Cohort Study (West Java, Indonesia) conducted from 2011 to 2016. Statistical analysis was performed using Receiver Operating Characteristics curve analysis with STATA version 15.

Results: Among prediabetes subjects (n = 371), the cut-off point of TyG index for regression from prediabetes to normoglycemic subjects was <4.51 [sensitivity, specificity, AUC (95%CI) 83.9%, 80.1%, 0.913 (0.875–0.943), respectively] and the cut-off point for progression from prediabetes to diabetes was >4.54 [80.0%, 73.1%, 0.858 (0.807–0.900)]. Among normoglycemic subjects (n = 1300), the cut-off point of TyG index for progression to prediabetes and diabetes were >4.44 [80.1%, 71.1%, 0.834 (0.812–0.854)] and >4.47 [80.6%, 80.8%, 0.909 (0.890–0.926)] respectively.

Conclusion: Based on sample of subjects evaluated between 2011 and 2016, TyG index appears to be a promising marker for glucose status conversion among reproductive-aged women in Jakarta, Indonesia.

1. Introduction

Type 2 Diabetes Mellitus (T2DM) is a major public health burden [1]. Patients with T2DM have an increased risk of cardiovascular disease, which is currently one of the leading causes of death and health expenditures in the world. Thus, prevention of T2DM should be one of the top priorities, especially to countries with limited health resources, including Indonesia. While the prevalence of diabetes in Indonesia is 10.9%, the prevalence of prediabetes, a precursor state of T2DM [2], has soared above 30% [3]. Without any

* Corresponding author. Division of Endocrinology Metabolism and Diabetes, Department of Internal Medicine, Dr. Cipto Mangunkusumo National Referral Hospital, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia.
** Corresponding author. Department of Public Health and Community Medicine, Epidemiology and Biostatistics sub-department, University of Sriwijaya, Palembang Indonesia.
E-mail addresses: iche.aliberty@gmail.com, icheandriyaniliberty@fk.unsri.ac.id (I.A. Liberty), dicky.tahapary@ui.ac.id (D.L. Tahapary).

https://doi.org/10.1016/j.dsx.2021.102280
1871-4021/

Table 1
Baseline characteristics of the 1300 normoglycemic subject.

Characteristics	Conversion Status		
	No conversion	Progression to Prediabetes	Progression to Diabetes
Age	6 (100%)	0 (0.0%)	0 (0.0%)
- 20–24 years	154 (83.7%)	30 (16.3%)	0 (0.0%)
- 25–29 years	203 (83.9%)	37 (15.3%)	2 (0.8%)
- 30–34 years	226 (79.0%)	56 (19.6%)	4 (1.4%)
- 35–39 years	211 (69.2%)	83 (27.2%)	11 (3.6%)
- 40–44 years	188 (67.9%)	75 (27.1%)	14 (5.1%)
- 45–49 years			
Occupation	714 (75.40%)	208 (21.96%)	25 (2.64.00%)
- Housewife	209 (77.70%)	54 (20.07%)	6 (2.23%)
- Informal sector	65 (77.38%)	19 (22.62%)	0 (0%)
- Formal sector			
Birth History Baby> 4 kg	854 (76.20%)	241 (21.50%)	26 (2.30%)
- Yes	52 (71.20%)	18 (24.70%)	3 (4.10%)
- No	35 (81.40%)	8 (18.60%)	0 (0.00%)
- Never Maternity			
Contraceptive Method	198 (72.0%)	69 (25.10%)	8 (2.90%)
- Hormonal	658 (77.50%)	171 (20.10%)	20 (2.40%)
- Non-Hormonal			
Menarche	19 (73.10%)	7 (26.90%)	0 (0.00%)
- ≤10 years	529 (76.00%)	152 (21.80%)	15 (2.20%)
- 11–13 years	394 (75.80%)	112 (21.50%)	14 (2.70%)
- 14–16 years	46 (79.30%)	10 (17.20%)	2 (3.40%)
- >16 years			
TyG Index			
- > 4.43	316 (62.20%)	173 (34.06%)	19 (5,7%)
- ≤ 4.43	672 (84.85%)	108 (13.64%)	12 (1.52%)
Total cholesterol			
- ≥200 mg/dl	368 (70.91%)	136 (26.20%)	15 (2.89%)
- < 200 mg/dl	620 (70.39%)	145 (18.57%)	16 (2.05%)
LDL			
- ≥100 mg/dl	759 (74.19%)	239 (23.36%)	25 (2.44%)
- < 100 mg/dl	229 (82.67%)	42 (15.16%)	6 (2.17%)
HDL			
- ≥ 50 mg/dl	635 (79.28%)	154 (19.23%)	12 (1.50%)
- < 50 mg/dl	353 (70.74%)	127 (25.45%)	19 (3.81%)
BMI			
- ≥ 23 kg/m^2	632 (72.06%)	219 (24.97%)	26 (2.96%)
- < 23 kg/m^2	356 (84.16%)	62 (14.66%)	5 (1.18%)
Waist Circumference			
- ≥ 80 cm	458 (69.92%)	173 (26.41%)	24 (3.66%)
- < 80 cm	530 (82.17%)	108 (16.74%)	7 (1.09%)
Systolic			
- ≥ 120 mmHg	449 (69.08%)	172 (26.46%)	29 (4.46%)
- < 120 mmHg	539 (82.92%)	109 (16.77%)	2 (0.31%)
Diastolic			
- ≥ 80 mmHg	402 (68.84%)	158 (27.05%)	24 (4.11%)
- < 80 mmHg	586 (81.84%)	123 (17.18%)	7 (0.98%)

health intervention, approximately 30% of people with prediabetes will experience diabetes within 5 years [4–6].

One of the priority group for diabetes prevention should be women at reproductive age. One out of 10 women globally already had diabetes and 2 out of 5 among them were in reproductive age. Glucose homeostasis and insulin sensitivity differ between sex — women are more prone to insulin resistance due to more adipose tissue, lower skeletal muscle mass, and higher circulating free fatty acid (FFA) compared to men [7]. Aside from that, previous studies showed that women with T2DM have higher morbidity and mortality due to cardiovascular disease. Hence, managing modifiable risk factors to prevent prediabetes and T2DM during preconception and pregnancy is an important strategy to prevent disease progression and future diabetic complications [1,8,9].

The intervention required to prevent diabetes might not be accessible in all community setting in Indonesia due to limited health facilities and human resources. Thus, focusing on a selected high-risk group of people should be a priority for diabetes preventions. This can be achieved by stratifying the risk of prediabetes progression to diabetes [10]. Given the fundamental role of insulin resistance (IR) in the development of prediabetes and diabetes, a simple and effective method to assess IR can be applied to predict glucose status conversion at community level. Triglyceride/Glucose Index (TyG Index) is a novel index for IR and can be easily applied in community setting with limited health facilities [11–15].

Diabetes prevention among reproductive-aged women should be a top priority. However, due to limitations in healthcare resources, aggressive prevention should target those with higher risk of progression. Our study aims to analyze TyG Index as a potential marker in predicting the conversion of prediabetes to diabetes and conversion of normoglycemic to prediabetes and diabetes among reproductive-aged women.

2. Materials and methods

2.1. Study design and populations

This is a retrospective cohort study using secondary data from

Table 2
Baseline characteristics of the 371 Prediabetes Subject.

Characteristics	Conversion Status		
	Regression to Normoglycemic	No Conversion	Progression to Diabetes
Age			
- 25–29 years	14 (48.3%)	11 (37.9%)	4 (13.8%)
- 30–34 years	27 (57.4%)	9 (19.1%)	11 (23.4%)
- 35–39 years	28 (38.4%)	34 (46.6%)	11 (15.1%)
- 40–44 years	48 (40.3%)	45 (37.8%)	26 (21.8%)
- 45–49 years	39 (37.9%)	38 (36.9%)	26 (25.2%)
Occupation	121 (42.46%)	110 (38.60%)	54 (18.95%)
- Housewife	17 (27.42%)	18 (29.03%)	17 (27.42%)
- Informal sector	7 (29.17%)	9 (37.50%)	7 (29.17%)
- Formal sector			
Birth History Baby> 4 kg	4 (21.10%)	11 (57.90%)	4 (21.10%)
- Yes	142 (43.20%)	120 (36.50%)	67 (20.40%)
- No	4 (40.00%)	3 (30.00%)	3 (30.00%)
- Never Maternity			
Contraceptive Method	120 (44.90%)	98 (36.70%)	49 (18.40%)
- Hormonal	21 (35.0%)	22 (36.67%)	17 (28.33%)
- Non-Hormonal			
Menarche	4 (36.40%)	5 (45.50%)	2 (18.20%)
- ≤10 years	84 (40.20%)	76 (36.40%)	49 (23.40%)
- 11–13 years	58 (46.80%)	43 (34.70%)	23 (18.50%)
- 14–16 years	10 (37.00%)	13 (48.10%)	4 (14.80%)
- >16 years			
TyG Index			
- > 4.54	42 (25.15%)	62 (37.13%)	63 (37.72%)
- ≤ 4.54	114 (55.88%)	75 (36.76%)	15 (7.35%)
Total cholesterol			
- ≥200 mg/dl	77 (37.75%)	77 (37.75%)	50 (24.51%)
- < 200 mg/dl	79 (47.31%)	60 (35.93%)	28 (16.77%)
LDL			
- ≥100 mg/dl	134 (41.61%)	119 (36.96%)	69 (21.43%)
- < 100 mg/dl	22 (44.90%)	18 (36.73%)	9 (18.37%)
HDL			
- ≥ 50 mg/dl	98 (48.51%)	76 (37.62%)	28 (13.86%)
- < 50 mg/dl	58 (34.32%)	61 (36.09%)	50 (29.59%)
BMI			
- ≥ 23 kg/m^2	105 (36.33%)	112 (38.75%)	72 (24.91%)
- < 23 kg/m^2	51 (62.20%)	25 (30.49%)	6 (7.32%)
Waist Circumference			
- ≥ 80 cm	83 (35.32%)	86 (36.60%)	66 (28.09%)
- < 80 cm	73 (53.68%)	51 (37.50%)	12 (8.82%)
Systolic			
- ≥ 120 mmHg	93 (35.63%)	104 (39.85%)	64 (24.52%)
- < 120 mmHg	63 (57.27%)	33 (30.0%)	14 (12.73%)
Diastolic			
- ≥ 80 mmHg	84 (35.29%)	96 (40.34%)	58 (24.37%)
- < 80 mmHg	72 (54.14%)	41 (30.83%)	20 (15.04%)

Bogor Non-Communicable Diseases (NCDs) Cohort Study which was conducted in five villages in Bogor, West Java, by the Ministry of Health of the Republic of Indonesia. The subjects of the study were recruited from 2011 to 2012 and the aim of the study was to evaluate several risk factors that contribute to the development of NCDs, such as T2DM, stroke, hypertension, and cardiovascular disease [16]. This study has been approved by the Ethical Committee Board of the Faculty of Public Health Universitas Indonesia with register number 271/H2·F10/PPM.00.02/2018.

We included reproductive-aged women (20–49 years) which were normoglycemic and in prediabetes state whose data was complete. Subjects who were pregnant; had T2DM or thyroid disease; consumed any drug that alter glucose and insulin metabolism (such as angiotensin-converting enzyme inhibitors [ACEI], angiotensin receptor blockers [ARB], or thiazide diuretics), as well as any drug that alter triglyceride, cholesterol, and HDL levels such as statins were excluded.

2.2. Measurements

The primary outcome of this study was glycemic conversion status of the subjects after 5 years of follow-up. We further divided the subjects into two groups which were Normoglycemic (no conversion and progression to be prediabetes or diabetes) and Prediabetes (regression, no conversion, and progression to be diabetes).

Baseline demographic characteristics were obtained using a standard questionnaire. Anthropometric measurements were performed by trained nurses according to standardized methods. Body weight was measured while the subjects were wearing light-weighted clothes and recorded to the nearest 0.1 kg, whereas body height was measured without shoes and recorded to the nearest 0.1 cm. Body mass index (BMI) was calculated by dividing body mass by the square of the body height (kg/m^2). BMI is divided into <23 kg/m^2 (normoweight) and ≥23 kg/m^2 (overweight and obese). Waist circumference measured circumferentially at the

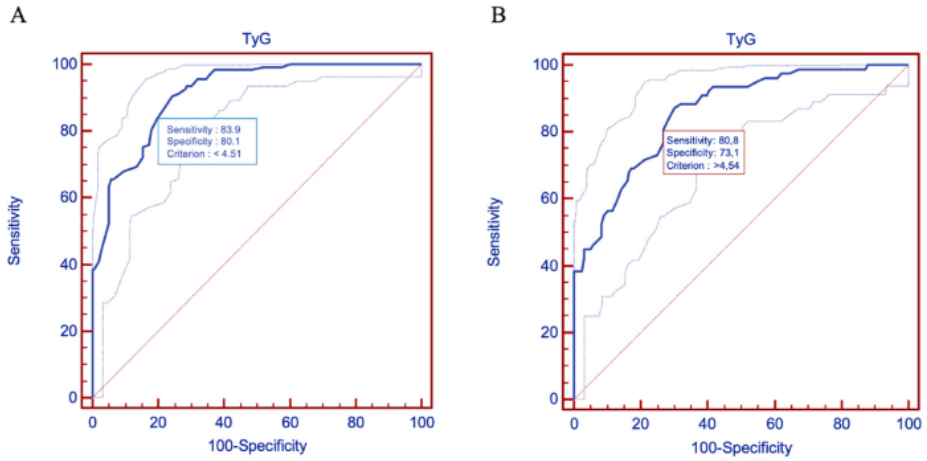

Fig. 1. ROC TyG Index Curve of Conversion Status on Prediabetes Subject. The cut-off point of TyG index for regression from prediabetes to normoglycemic status was <4.51 (A) and the cut-off point for progression from prediabetes to diabetes status was >4.54 (B).

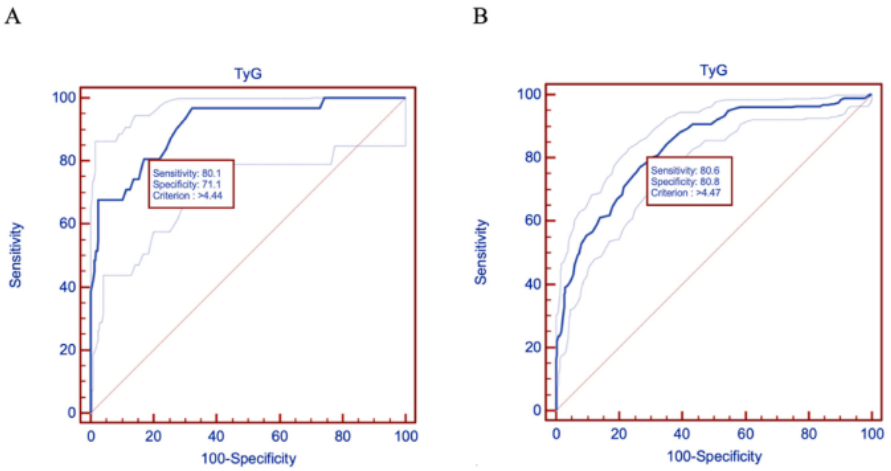

Fig. 2. ROC TyG Index Curve of Conversion Status on Normoglycemic Subject. The cut-off point of TyG index for progression to prediabetes and diabetes were >4.44 (A) and >4.47 (B).

midpoint between the lower rib margin (arcus costae) and the upper iliac border. Measurements were made 2 times; when there was a difference of more than 3 cm, then the mean of the 2 measurements was taken as a result (the two closest measurements) and then categorized into <80 cm (normal) and ≥80 cm (elevated). Blood specimens were drawn after at least 8 h of overnight fasting. Routine laboratory tests which were fasting plasma glucose (FPG), oral glucose tolerance test (OGTT), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured using standardized method and commercial reagents in a qualified laboratory.

2.3. Definitions

Diabetes was defined as FPG level ≥126 mg/dL (7.0 mmol/L), 2-h plasma glucose following an OGTT ≥200 mg/dL (11.1 mmol/L), random blood glucose >200 mg/dL (11.1 mmol/L), or HbA1c ≥ 6.5%. Prediabetes comprises of any of the following three parameters: impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and elevated glycated hemoglobin (HbA1c) [2]. IGT was defined as OGTT of 140–199 mg/dL (7.8–11 mmol/L) and IFG was defined as FPG level of 100–125 mg/dL (5.6–7.0 mmol/L). Subjects with HbA1c ranged 5.7–6.4% were classified as prediabetes.

TyG Index is calculated by the following formula [11].

TyG Index = Ln (fasting glucose (mg/dL) x triglycerides (mg/dL)/2).

2.4. Statistical analysis

The data were analyzed using STATA version 15 (College Station, Texas 77845 USA) and presented in values (percentage) for categorical data. The cut-off point for TyG Index predictive value on glucose status conversion was analyzed using Receiver Operating Characteristics (ROC) curve and determined by optimum values of sensitivity and specificity.

3. Results

A total of 1300 normoglycemic subjects (Table 1) and 371 prediabetes subjects (Table 2) were included in this study. After 5 years of follow up, among prediabetes subjects, 42.05% (156/371) regressed to normoglycemic, 36.93% (137/371) remained in prediabetes state, and 21.02% (78/371) progressed to diabetes. Among normoglycemic subjects, 2.38% (31/1300) progressed to diabetes, 21.62% (281/1300) progressed to prediabetes state, and 76% (988/1300) remained in normoglycemic state.

In prediabetes group, the percentage of subjects who had regression to normoglycemic state decreased with age; and the percentage of subjects who had progression to diabetes increased with age. Likewise, in normoglycemic subjects, the percentage of subjects who did not experience conversion decreased with age; and the percentage of subjects experienced progression to diabetes increased with age. Another concern was in prediabetes group aged 30−34 years, 23.4% of the subjects experienced progression to diabetes and only 19.1% remained in prediabetes state. These were possible because there are many subjects in that age range who were pregnant which triggered an increase in body fat composition.

In prediabetes subjects, the highest proportions of regression to normoglycemic were those who were self-employed (43.50%) and married (42.60%). Most of prediabetes subjects experiencing the progression to diabetes were non-domestic workers (2.40%). In normoglycemic subject, the highest proportion of subjects with progression to diabetes was in subjects with history of menarche at the age of 16 years old and above (2.70%). The largest proportion of prediabetes subjects with regression to normoglycemic state was those with hormonal contraceptive methods. Otherwise, majority of subjects progressed to diabetes were using non-hormonal contraceptive methods. In normoglycemic subjects, the largest proportion of subjects who progressed to diabetes was subjects using hormonal contraceptive methods. The results of this study indicate that the impact of the contraceptive method on blood glucose is not consistent.

Based on ROC analysis among prediabetes subjects, the cut-off point of TyG index for regression from prediabetes to normoglycemic status was <4.51 [sensitivity, specificity, AUC (95%CI) 83.9%, 80.1%, 0.913 (0.875−0.943), respectively] and the cut-off point for progression from prediabetes to diabetes status was >4.54 [80.0%, 73.1%, 0.858 (0.807−0.900)] (Fig. 1). Based on ROC analysis among normoglycemic subjects, the cut-off point of TyG index for progression to prediabetes and diabetes were >4.44 [80.1%, 71.1%, 0.834 (0.812−0.854)] and >4.47 [80.6%, 80.8%, 0.909 (0.890−0.926)] respectively (Fig. 2).

About 55.8% of prediabetic subjects who had regression to normoglycemic had TyG index ≤4.54, normal lipid profile, normal systolic and diastolic blood pressure, and higher HDL compared to those who progressed to diabetes. Likewise, in the normoglycemic subjects, the majority of normoglycemic subjects who had no glucose status conversion (84.58%) had TyG index ≤4.43, normal total cholesterol and LDL, normal systolic and diastolic blood pressure, and high HDL.

4. Discussion

Our study observed that among reproductive-aged women, the TyG Index was a good diagnostic marker not only for prediabetes progression to diabetes but also for regression to normoglycemic state. In our study population, the TyG Index was also good at determining progression from normoglycemic state to prediabetes and diabetes.

Our findings were in parallel with previous study which reported that high FPG and high serum fasting triglycerides were independent predictors of the progression from prediabetes to diabetes, whereas normal FPG and low serum fasting triglycerides were independent predictors of regression from prediabetes to normoglycemic state. Both FPG and triglycerides were used in the development of TyG index formula [17]. Thus, using TyG index, which is a surrogate marker of insulin resistance, might better predict the progression or regression of glycemic status rather than using each parameter separately.

The high accuracy of TyG index in predicting glycaemic status conversion was in accordance with its high predictive value compared to Hyperinsulinemic-Euglycemic Clamp (HEC) in previous study [11]. TyG Index was also found to be strongly correlated with Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) [22], a commonly used formula for assessing insulin resistance in clinical practice [11,18]. The use of TyG at community level will be much more simple than HEC and HOMA-IR. The TyG index can potentially be used to stratify high-risk group among those with normoglycemic and prediabetes state, hence intensive intervention can be performed. This can potentially beneficial as in many Low-to-Middle-Income Countries (LMICs), including Indonesia, the already limited healthcare funding for T2DM prevention can be focused on those high-risk group of people.

The accuracy of TyG index for predicting glycaemic conversion status might be related with the fact that the formula not only including the FPG as glycaemic parameter but also TG, which is a surrogate marker for insulin resistance-associated changes in lipid metabolism. Hypertriglyceridemia causes high FFA transport to the liver resulting in high hepatic glucose output. High plasma FFA concentrations also decrease insulin response of skeletal muscle and liver [19,20]. Lipotoxicity caused decreased expression of proliferator activator γ co-activator 1α (PGC-1α), which has an active role on regulation of muscle mitochondrial function as a response to the lipid levels [21,22]. FFA also directly alter the insulin signalling cascade, decrease activation of insulin-1 receptors, and decreae phosphatidylinositol-3 kinase activity. It is important to maintain a normal triglyceride level to improve the insulin sensitivity and prevent the conversion of prediabetes into diabetes [23].

After 5 years of follow up in our study, 21.62% of normoglycemic subjects progressed to prediabetes state and 2.38% progressed to diabetes. Among prediabetes subjects, 21.02% progressed to diabetes. Previous studies reported that people with prediabetes will experience conversion to diabetes in 4−10 years with a risk of 25%−65% compared to people with normoglycemic which are only 5% [24−26]. Our results showed lower progression compared to the study among Asian Indian women, which reported that 26.9% normoglycemic subjects converted to prediabetes and 20.1% progressed to diabetes. Among those with prediabetes subjects in their study, 60.8% converted to diabetes and 15.2% regressed to normoglycemic state. The differences may be caused not only by their longer period of follow up (10 years) compared to our study but also differences in race [27]. It is also important to note that in our study population, more than 42% of subjects with prediabetes regress to normoglycemic. This finding was relatively higher in comparison to previous study. Despite not being assessed in our study, the presence of NCDs health post (Posbindu PTM) in our study area which provided education among those with prediabetes and diabetes might contribute to this finding.

This study has some limitations. There might be some differences of the results in Indonesian population considering the country's high ethnic diversity. Second, the follow-up in this study was done in a relatively short period of time of 5 years. Nevertheless, our study is the first community-based large-scale longitudinal study in Indonesia.

In summary, the TyG index is a good marker for predicting glucose conversion among reproductive-aged women at

community setting in Indonesia. Further multicenter studies involving different ethnicities and longer follow-up period are needed to confirm the performance of TyG Index.

Declaration of competing interest

All the authors have disclosed no potential conflicts of interest relevant to this article and have read and accepted the journal's policy on conflicts of interest, as well as the journal's authorship agreement.

Acknowledgments

We would like to thank Universitas Indonesia for publishing this article and Indonesia Endowment Fund for Education (LPDP RI) for financing PhD scholarship. The authors also convey their appreciation for Cindy Astrella for her assistance in writing the manuscript.

References

[1] International Diabetes Federation. Global perspectives on diabetes. 2017.
[2] Yudkin JS. Prediabetes": are there problems with this label? Yes, the label creates further problems! Diabetes Care 2016 Aug;39:1468–71.
[3] Development NHIR and National Health Institute Research and Development. Jakarta: Ministry of health of the republic Indonesia. 2018.
[4] Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med n.d.;346:393–403.
[5] Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med n.d.;344; 1.
[6] Marshall C, Adams S, Dyer W, Schmittdiel J. Opportunities to reduce diabetes risk in women of reproductive age: assessment and treatment of prediabetes within a large integrated delivery system. Women's Heal Issues n.d.;27;6:666–672.
[7] Avery F, Kraja BMBM. Genotype-by-sex interaction in the aetiology of type 2 diabetes mellitus: support for sex- specific quantitative trait loci in Hypertension Genetic Epidemiology Network participants. Diabetologia n.d.;49.
[8] Liberty IA, Kodim N. {ASSESS} {prediabetes} {risk}, {as} a {golden} {period} {for} {prevention} {OF} {diabetes}. Asian J Pharmaceut Clin Res 2017;10:349. https://doi.org/10.22159/ajpcr.2017.v10i6.18215.
[9] American Diabetes Association. Standards of medical care in diabetes. USA. 2018.
[10] DeFronzo RA, Tripathy D. Skeletal muscle insulin resistance is the primary defect in type 2 diabetes. Diabetes Care 2009;32:S157–63. https://doi.org/10.2337/dc09-s302.
[11] Guerrero-Romero F, Simental-Mendi\'a LE, Gonza\'lez-Ortiz M, Martí\'nez-Abundis E, Ramos-Zavala MG, Hernа\'ndez-Gonza\'lez SO, et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. J Clin Endocrinol Metab 2010;95:3347–51. https://doi.org/10.1210/jc.2010-0288.
[12] Sánchez-Íñigo L, Navarro-González D, Fernández-Montero A, Pastrana-Delgado J, Mart\'\inez JA. The {TyG} index may predict the development of cardiovascular events. Eur J Clin Invest 2016;46:189–97. https://doi.org/10.1111/eci.12583.
[13] Nor NSM, Lee S, Bacha F, Tfayli H, Arslanian S. Triglyceride glucose index as a surrogate measure of insulin sensitivity in obese adolescents with normoglycemia, prediabetes, and type 2 diabetes mellitus: comparison with the hyperinsulinemic-euglycemic clamp. Pediatr Diabetes 2015;17:458–65. https://doi.org/10.1111/pedi.12303.
[14] Gao Y-X, Man Q, Jia S, Li Y, Li L, Zhang J. The fasting serum triglyceride levels of elderly population with different progression stages of diabetes mellitus in China. J Diabet Complicat 2017;31:1641–7. https://doi.org/10.1016/j.jdiacomp.2017.08.011.
[15] Lee EY, Yang HK, Lee J, Kang B, Yang Y, Lee S-H, et al. Triglyceride glucose index, a marker of insulin resistance, is associated with coronary artery stenosis in asymptomatic subjects with type 2 diabetes. Lipids Health Dis 2016;15:155. https://doi.org/10.1186/s12944-016-0324-2.
[16] Nusrianto R, Ayundini G, Kristanti M, Astrella C, Amalina N, Muhadi, et al. Visceral adiposity index and lipid accumulation product as a predictor of type 2 diabetes mellitus: the Bogor cohort study of non-communicable diseases risk factors. Diabetes Res Clin Pract 2019;155:107798. https://doi.org/10.1016/j.diabres.2019.107798.
[17] de Abreu L, Holloway KL, Kotowicz MA, Pasco JA. Dysglycaemia and other predictors for progression or regression from impaired fasting glucose to diabetes or normoglycaemia. J Diabetes Res 2015;2015:1–8. https://doi.org/10.1155/2015/373762.
[18] Salazar J, Bermúdez V, Calvo M, Olivar LC, Luzardo E, Navarro C, et al. Optimal cutoff for the evaluation of insulin resistance through triglyceride-glucose index: a cross-sectional study in a Venezuelan population. F1000Research 2018;6:1337. https://doi.org/10.12688/f1000research.12170.3.
[19] Parhofer KG. Interaction between glucose and lipid metabolism: more than diabetic dyslipidemia. Diabetes Metab J 2015;39:353–62. https://doi.org/10.4093/dmj.2015.39.5.353.
[20] Tune JD, Goodwill AG, Sassoon DJ, Mather KJ. Cardiovascular consequences of metabolic syndrome. Transl Res 2017;183:57–70. https://doi.org/10.1016/j.trsl.2017.01.001.
[21] Wang TJ, Larson MG, Vasan RS, Cheng S, Rhee EP, McCabe E, et al. Metabolite profiles and the risk of developing diabetes. Nat Med 2011;17:448–53. https://doi.org/10.1038/nm.2307.
[22] Eldor R, Norton L, Fourcaudot M, Galindo C, DeFronzo RA, Abdul-Ghani M. Increased lipid availability for three days reduces whole body glucose uptake, impairs muscle mitochondrial function and initiates opposing effects on {PGC}-1$\upalpha$ promoter methylation in healthy subjects. PloS One 2017;12:e0188208. https://doi.org/10.1371/journal.pone.0188208.
[23] Makimura H, Stanley TL, Suresh C, De Sousa-Coelho AL, Frontera WR, Syu S, et al. Metabolic effects of long-term reduction in free fatty acids with acipimox in obesity: a randomized trial. J Clin Endocrinol Metab 2016;101:1123–33. https://doi.org/10.1210/jc.2015-3696.
[24] Garber AJ, Handelsman Y, Einhorn D, Bergman DA, Bloomgarden ZT, Fonseca V, et al. ACE/AACE consensus statement diagnosis and management of prediabetes in the continuum of Hyperglycemia — when do the risks of diabetes Begin ? A consensus statement from the. American College of Endocrinology and the American Association of Clinical Endo 2008;14:933–46.
[25] Geiss LS, James C, Gregg EW, Albright A, Williamson DF, Cowie CC. Diabetes risk reduction behaviors among U.S. Adults with prediabetes. Am J Prev Med 2010;38:403–9. https://doi.org/10.1016/j.amepre.2009.12.029.
[26] Tuso P. Prediabetes and lifestyle modification: time to prevent a preventable disease. Perm J 2014;88–93. https://doi.org/10.7812/tpp/14-002.
[27] Anjana RM, Shanthi Rani CS, Deepa M, Pradeepa R, Sudha V, Divya Nair H, et al. Incidence of diabetes and prediabetes and predictors of progression among asian Indians: 10-year follow-up of the Chennai urban rural epidemiology study (CURES). Diabetes Care 2015;38:1441–8. https://doi.org/10.2337/dc14-2814.

Triglyceride/Glucose Index (TyG Index) as a marker of glucose status

ORIGINALITY REPORT

4%
SIMILARITY INDEX

PRIMARY SOURCES

1	David Navarro-González, Laura Sánchez-Íñigo, Juan Pastrana-Delgado, Alejandro Fernández-Montero, J. Alfredo Martinez. "Triglyceride–glucose index (TyG index) in comparison with fasting plasma glucose improved diabetes prediction in patients with normal fasting glucose: The Vascular-Metabolic CUN cohort", Preventive Medicine, 2016 Crossref	75 words — 2%
2	e-sciencecentral.org Internet	22 words — 1%
3	jmir.org Internet	22 words — 1%
4	"Posters", Basic & Clinical Pharmacology & Toxicology, 06/22/2010 Crossref	20 words — 1%

EXCLUDE QUOTES	OFF	EXCLUDE MATCHES	< 1%
EXCLUDE BIBLIOGRAPHY	ON		