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Predictive Value of the Triglyceride-Glucose Index and Small Dense LDL-C for Metabolic Syndrome in Young Syrian Women

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ABSTRACT

Background: *Research on metabolic syndrome (MetS) in young women within the Eastern Mediterranean is limited. This study assessed MetS prevalence and risk factors among female pharmacy students in Syria, while evaluating the diagnostic utility of the Triglyceride-Glucose (TyG) index and small dense LDL-C (sdLDL-C).*

Methods: *A cross-sectional study was conducted with 129 women (ages 20–30) at Arab International University. MetS was defined by International Diabetes Federation (IDF) criteria. Data collection included structured questionnaires, anthropometric measurements, and fasting blood analysis.*

Results: *The prevalence of MetS was 7.0%. Central obesity (waist circumference ≥80 cm) was the most common risk factor, present in 100% of MetS cases, followed by elevated blood pressure and low HDL-C. Notable lifestyle risks included physical inactivity (50.39%) and frequent fast-food consumption (34.11%). Participants with at least one MetS risk factor had significantly higher TyG index (8.9 vs. 8.02, p=0.003) and sdLDL-C levels (35.2 vs. 26.13 mg/dL, p=0.007) than those with no risk factors. The TyG index correlated strongly with triglycerides (r=0.83) and sdLDL-C (r=0.59).*

Conclusion: *Young Syrian women face a significant burden of metabolic risk associated with sedentary lifestyles. The TyG index is a simple, cost-effective tool for early insulin resistance screening. Integrating these biomarkers into routine clinical practice could improve early detection and prevention strategies in high-risk populations.*

Keywords

Metabolic Syndrome, Insulin Resistance, Triglyceride-Glucose Index (TyG), Small Dense LDL-C, Syria, University Students, Early Detection.

Abbreviation

AIU: Arab International University, BMI: Body Mass Index kg/m^2, BP: Blood Pressure mmHg, CVD: Cardiovascular Disease, EMR: Eastern Mediterranean Region, FPG: Fasting Plasma Glucose mg/dl, HDL-C: High-Density Lipoprotein Cholesterol mg/dl, HOMA-IR: Homeostasis Model Assessment for Insulin Resistance Index Unitless), IDF: International Diabetes Federation, lbLDL-C: Large-buoyant Low-Density Lipoprotein Cholesterol mg/dl, LDL-C: Low-Density Lipoprotein Cholesterol mg/dl, MetS: Metabolic Syndrome, sdLDL-C: Small dense Low-Density Lipoprotein Cholesterol mg/dl, T2DM: Type 2 Diabetes

Mellitus, TC: Total Cholesterol mg/dl, TG: Triglycerides mg/dl, TyG Index: Triglyceride-Glucose Index Index (Unitless), WC: Waist Circumference cm.

Introduction

Metabolic Syndrome (MetS) is a critical public health challenge characterized by a cluster of interrelated dysregulations, including visceral obesity, hypertension, atherogenic dyslipidemia, and dysglycemia [1]. Rather than occurring in isolation, these conditions synergistically amplify the risk of type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD), contributing significantly to global morbidity [1,2]. The pathogenesis of MetS is multifactorial, driven by a complex interplay of genetic predisposition, chronic inflammation, and modifiable lifestyle factors-all centred around insulin resistance as the primary pathophysiological hub [3].

The International Diabetes Federation (IDF) defines MetS by the presence of central obesity (waist circumference ≥80 cm for Europid women) plus any two of the following: elevated triglycerides, reduced high-density lipoprotein cholesterol (HDL-C), hypertension, or impaired fasting glucose [4]. This framework positions central adiposity not merely as a symptom, but as a core driver of the metabolic perturbations that underpin the syndrome.

The burden of MetS is disproportionately high in the Eastern Mediterranean Region (EMR), which reports the world's second-highest prevalence of T2DM (~25%) [5]. In Syria, a pre-crisis study in 2016 revealed an alarming MetS prevalence of 39.6% among adults, with hypertension and central obesity identified as the most common features [2]. While traditionally associated with middle age, MetS is increasingly identified in younger adults and university students [3]. This shift is strongly linked to the adoption of "Westernized" behaviors, including sedentary routines, the consumption of energy-dense fast food, and waterpipe smoking [1,6]. Identifying metabolic risk in this demographic is vital for implementing timely, cost-effective interventions before long-term complications arise.

Beyond classical diagnostic criteria, emerging biomarkers offer enhanced insight into early risk stratification. The Triglyceride-Glucose (TyG) index has surfaced as a simple, inexpensive surrogate for insulin resistance, with evidence suggesting it may equal or surpass the Homeostasis Model Assessment (HOMA-IR) in predicting incident diabetes and CVD [7]. Similarly, small dense low-density lipoprotein cholesterol (sdLDL-C) has garnered attention as a highly atherogenic subclass. These particles are more prone to oxidation and arterial wall penetration, representing a significant cardiovascular risk even when traditional LDL-C levels appear normal [8,9].

Despite the high regional prevalence of metabolic disorders, data regarding young Syrian women remain strikingly scarce. This population represents a critical demographic for study, as they are at a formative life stage where early metabolic deviations may first become detectable. Given the scarcity of metabolic data for young Syrian adults, this study aimed to determine the prevalence of MetS and its associated risk factors among female pharmacy students. A secondary aim was to evaluate the associative role of the TyG index and sdLDL-C as cost-effective screening tools for insulin resistance. These findings are intended to guide the development of targeted health interventions and screening protocols to mitigate the escalating burden of cardiovascular disease and diabetes in the region.

Materials and Methods

Study Design and Ethical Considerations

A cross-sectional study was conducted between May and September 2024 at the Arab International University (AIU) in Daraa, Syria. The study protocol was approved by the AIU Research Ethics Committee (Project No. 9-5-20-5-2024). All participants provided written informed consent after receiving a detailed explanation of the study objectives, procedures, risks, and benefits. Data were anonymized to ensure participant confidentiality.

Study Population and Sampling

Using a convenience sampling approach, 129 female pharmacy students aged 18–30 were enrolled. Inclusion criteria required participants to be apparently healthy, non-pregnant, and non-lactating. Exclusion criteria included a history of malignancy, myocardial infarction, hypothyroidism, or any acute illness at the time of data collection.

Data Collection

Questionnaire: A pre-tested, interviewer-administered questionnaire collected data on:

- **Demographics:** Age and family history of type 2 diabetes (T2DM) or cardiovascular disease (CVD) in first-degree relatives.
- **Lifestyle Factors:** Smoking status (cigarettes/waterpipe), frequency of fast-food consumption, and physical activity. Participants were classified as "inactive" if they engaged in <60 minutes of moderate-intensity activity per week.

Anthropometric and Clinical Measurements

Measurements were performed by trained personnel using calibrated equipment. Height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively, with participants in light clothing and without shoes. Body Mass Index (BMI) was calculated as weight (kg)/height (m^2). Waist circumference (WC) was measured at the midpoint between the lowest rib and the iliac crest. Blood pressure (BP) was measured using an automated sphygmomanometer (boso-medimat, Germany) after a 15-minute rest; the average of two readings was recorded.

Biochemical Analysis

After a 10–12 hour fast, 5 mL of venous blood was collected and centrifuged (3000× g for 15 minutes at 20°C). Serum was stored at −20°C. Total cholesterol (TC), triglycerides (TG), and HDL-C were measured using enzymatic assays (Mindray, China). Fasting plasma glucose (FPG) was determined via the glucose oxidase-peroxidase method (BioSystems, Spain).

Derived Indices and Definitions

- **LDL-C:** Calculated using the Friedewald formula (TC - HDL-C - TG/5) for TG <400 mg/dL.
- **TyG Index:** Calculated as $L[TG(mg/dL)\times FPG(mg/dL)]/2$.
  sdLDL-C: Estimated using Sampson's equations based on standard lipid parameters and large-buoyant LDL (lbLDL-C) calculations:

1. LDL-C = Total-C/0.948 - HDL-C/0.971 - (TG/8.56 + TG × non HDL - C/2140 - TG²/16100) - 9.44
2. lbLDL-C = 1.43 × LDL-C - 0.14 × (ln (TG) × LDL-C) - 8.99
3. sdLDL-C = LDL-C - lbLDL-C

- **MetS Definition:** Defined per IDF criteria for Europids: WC ≥80 cm plus at least two of the following: TG ≥150 mg/dL, HDL-C <50 mg/dL, BP ≥130/85 mmHg, or FPG ≥100 mg/dL (or treatment for these conditions).

Statistical Analysis

Continuous variables were summarized by frequencies and mean/standard deviation as appropriate. Data normality was assessed using Shapiro-Wilk and d'Agostino-Pearson tests. Differences between groups were evaluated using linear regression, with residuals tested for normality and homoscedasticity (Breusch-Pagan test). For non-normally distributed data, Kendall's tau-b correlation or Fisher's Exact Test was employed. A p-value <0.05 was considered statistically significant. All analyses were performed using Microsoft Excel 2007.

Results

Baseline Characteristics and Lifestyle Factors

Tables 1 and 2 summarize the biochemical characteristics and health determinants of the 129 participants. Most participants fell within healthy reference ranges for fasting glucose (89.15%) and triglycerides (97.67%). However, significant deviations were noted in lifestyle and anthropometric measures: 50.39% of the students reported physical inactivity (<1 hour/day) and 34.11% consumed fast food at least five times per month. Additionally, a high prevalence of family history for cardiovascular disease (51.16%) and type 2 diabetes (50.39%) was observed.

Table 1: Biochemical Profile of Participants (n=129).

Parameter	Reference Range	No Within Range	Percentage
Fasting Glucose	70–99 mg/dL	115	89.2%
Total Cholesterol	< 200 mg/dL	115	89.2%
HDL-C	> 40 mg/dL	103	79.8%
Triglycerides	< 150 mg/dL	126	97.7%
LDL-C	< 130 mg/dL	109	84.5%
sdLDL-C	< 34 mg/dL	113	87.6%
TyG Index	< 8.8	125	96.9%

No, Number of participant whose results fall within reference ranges; TC, Total Cholesterol; HDL-C, Hight Density Lipoprotein Cholesterol; TG, Triglycerides; LDL-C, Low density lipoprotein cholesterol; calculated, sdLDL-C, Low Density Lipoprotein Cholesterol and small dense LDL Cholesterol, respectively, both are calculated using NIH-Sampson Equation; TyG, equal to: ln((FBG x TG)/2).

Table 2: Clinical, anthropometric, and lifestyle characteristics (n=129).

Characteristic	Category/Range	n (%)
Clinical		
Systolic BP	90–129 mmHg	112 (88.83%)
Diastolic BP	60–84 mmHg	112 (88.83%)
Anthropometric		
Waist Circumference	<80 cm	84 (65.12%)
BMI	18.5–24.9 kg/m²	71 (55.04%)
Lifestyle		
Physical Inactivity	<1 hour/week	65 (50.39%)
High Fast Food Intake	≥5 meals/month	44 (34.11%)
Smoking (Hookah)	Yes	23 (17.83%)
Family History		
CVD	Yes	66 (51.16%)
T2DM	Yes	64 (50.39%)

No, Number of participants whose results fall within reference range; S, Systolic; D, Diastolic; BP, Blood pressure; BMI, Body mass index; CVD, Cardiovascular diseases; T2DM, Type 2 Diabetes Mellitus. No; Participant results within reference ranges.

Prevalence of Metabolic Syndrome (MetS)

Prevalence data for MetS among the Syrian pharmacy students are detailed in Table 3. According to IDF criteria, the overall prevalence of MetS in this cohort was 7.0% (n=9). Among the individual components, low HDL-C (<50 mg/dL) was the most frequent abnormality (45.7%), followed by central obesity (34.8%). All nine MetS cases exhibited a waist circumference ≥80 cm, which was mostly accompanied by elevated blood pressure (n=9) and low HDL-C (n=7).

Table 3: Prevalence of MetS components (IDF Criteria).

MetS Component	Threshold	n (%)
Central Obesity	Waist circumference ≥80 cm	45 (34.8%)
Low HDL-C	<50 mg/dL	59 (45.7%)
Elevated BP	≥130/85 mmHg	12 (9.3%)
Elevated FPG	≥100 mg/dL	10 (7.75%)
Elevated TG	≥150 mg/dL	3 (2.3%)

Mets, Metabolic Syndrome; IDF, International Diabetes Federation; S, Systolic; D, Diastolic; BP, Blood Pressure.

Performance of Emerging Biomarkers (TyG and sdLDL-C)

Table 4 provides a detailed comparison of emerging biomarkers, specifically TyG and sdLDL-C, within the cohort of Syrian pharmacy students. Participants with at least one MetS risk factor exhibited significantly higher mean levels of the TyG index (8.9 ± 0.4 vs. 8.02 ± 0.41, p=0.003) and sdLDL-C (35.2 ± 8.5 vs. 26.13 ± 8.4 mg/dL, p=0.007) compared to those with no risk factors.

Correlation analysis revealed that the TyG index had a very strong positive correlation with TG (r=0.83, p<0.001) and a strong correlation with sdLDL-C (r=0.59, p<0.001). Conversely, TyG showed a significant inverse correlation with HDL-C (r=-0.30, p=0.001).

Table 4: Correlation matrix of metabolic risk factors.

Variable 1	Variable 2	Test	Correlation (r)	p-Value
TyG Index	Triglycerides	Kendall's tau	0.83	<0.001
TyG Index	sdLDL-C	Kendall's tau	0.59	<0.001
TyG Index	HDL-C	Linear Reg.	-0.30	0.001
sdLDL-C	Triglycerides	Kendall's tau	0.65	<0.001
Waist Circ.	sdLDL-C	Kendall's tau	0.16	0.006
Waist Circ.	HDL-C	Linear Reg.	-0.20	0.026

HDL-C; High Density Lipoprotein Cholesterol; Cir, Circumference; sdLDL-C; Small Dense Low Density Lipoprotein Cholesterol; TyG, Triglycerides Glucose Index; TG, Triglycerides; Reg, Linear Regression; Tau, Kendall's tau-b; CC, coefficient correlation.

Discussion

This pilot cross-sectional study provides a critical epidemiological perspective on the metabolic health of young Syrian women-a demographic historically underrepresented in cardiometabolic research. We identified a metabolic syndrome (MetS) prevalence of 7.0% (n=9) based on International Diabetes Federation (IDF) criteria. While considerably lower than the pre-crisis national adult prevalence of 39.6% (2), this finding confirms that MetS is already emerging in young, ostensibly healthy populations.

The lifestyle profile of this cohort is concerning. Over half of the participants reported physical inactivity (50.39%), while 34.11% reported frequent fast-food consumption. These modifiable drivers of insulin resistance, coupled with a high prevalence of family history for type 2 diabetes (50.39%), create a high-risk context for early metabolic dysfunction [10,11]. Notably, hookah smoking (17.83%) was significantly more common than cigarette smoking (3.88%). This aligns with regional research suggesting hookah use is a significant, yet often overlooked, risk factor for MetS and obesity [12].

Among the conventional IDF criteria, low HDL-C (<50 mg/dL) was the most prevalent abnormality, affecting 45.7% of participants. This rate is consistent with regional trends [13] and is particularly clinically relevant, as low HDL-C in young women is a strong predictor of future diabetes [14].

Elevated waist circumference (≥80 cm) affected 34.8% of the cohort. We observed a significant correlation between waist circumference and BMI ($r = 0.59$, $p < 0.05$), supporting previous findings that central adiposity is a primary driver of MetS in Syrian youth [15]. Conversely, the prevalence of hypertension (5.42%), elevated fasting glucose (7.75%), and hypertriglyceridemia (2.3%) was relatively low compared to studies in other regions [13,16]. The low rate of hypertriglyceridemia may be attributed to the traditional Mediterranean diet, which is protective against lipid dysregulation [17].

The core contribution of this study is the evaluation of the Triglyceride-Glucose (TyG) index and small dense LDL-C (sdLDL-C). Participants with at least one MetS risk factor exhibited significantly higher mean levels of both markers ($p < 0.01$).

The TyG index serves as a composite reflection of hepatic triglyceride overproduction and impaired glucose regulation. Our correlation analyses map a clear pathophysiological pathway: visceral adiposity (waist circumference) correlates with the TyG index, which in turn shows an exceptionally strong relationship with triglycerides ($r = 0.83$) and sdLDL-C ($r = 0.59$). This triad—linking central obesity to insulin resistance and a pro-atherogenic lipid profile—validates TyG as a robust marker of metabolic disturbance [18,19].

Clinical Implications

The TyG index warrants emphasis as a transformative clinical tool. Because it is derived from routine, inexpensive fasting measurements, it offers a cost-effective alternative to complex assays like HOMA-IR. In this study, a TyG value of 8.9 ± 0.4 effectively identified individuals at risk, making it a scalable solution for large-scale screenings, such as university health campaigns [20].

Furthermore, the elevation of sdLDL-C in this young cohort signals early vascular risk. While sdLDL-C is difficult to measure directly, its strong correlation with the TyG index suggests that TyG can serve as a practical surrogate marker for atherogenic dyslipidemia [21]. Using these markers in tandem could allow for earlier intervention in high-risk young populations before overt cardiovascular disease develops.

Conclusion

This study documents a tangible metabolic burden in young Syrian women, driven by a synergy of lifestyle factors and genetic predisposition. Beyond reporting a 7.0% MetS prevalence, we provide evidence that the TyG index and sdLDL-C are sensitive barometers of early-stage insulin resistance and vascular risk. The interplay between visceral adiposity and these biomarkers confirms a clear pathophysiological pathway toward atherogenic dyslipidemia in this cohort. As a simple, scalable, and inexpensive metric, the TyG index represents a transformative opportunity for clinical screening, allowing for the identification and mitigation of metabolic risk at a formative life stage.

Limitations

While this pilot study offers valuable insights into the metabolic risk profiles of young Syrian women, several limitations warrant consideration. Primarily, the use of convenience sampling among female pharmacy students at a single institution limits the external validity of the findings. Furthermore, the cross-sectional design precludes causal inferences; longitudinal research remains essential to determine the predictive capacity of the TyG index and sdLDL-C for incident metabolic disease. Additionally, the modest sample size (n=129) may have constrained the statistical power to identify subtle associations. Data regarding lifestyle factors, such as diet and physical activity, were subject to recall and social desirability biases inherent in self-reported measures. Finally, while the Sampson equation provides a validated, practical alternative for resource-limited settings, it serves as an estimate rather than a direct quantification of sdLDL-C, which may lack the

precision of advanced laboratory techniques.

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