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CASE REPORT **OPEN ACCESS**

Triglyceride-Glucose, TG/HDL-C Ratio, and Lipoprotein(a) as Early Cardiovascular Risk Markers in Hypertensive Patients: Impact of Lifestyle and Pharmacological Interventions

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ABSTRACT

Background: Cardiovascular disease (CVD) is a leading cause of mortality, with diabetic dyslipidemia, hypertension, and elevated homocysteine and lipoprotein(a) [Lp(a)] as key risk factors. The triglyceride/HDL cholesterol (TG/HDL-C) ratio and triglyceride-glucose (TyG) index are emerging cost-effective markers of insulin resistance and CVD risk.

Objective: To evaluate the impact of a 3-month lifestyle and pharmacological intervention on homocysteine, body mass index (BMI), glycated hemoglobin (HbA1c), postprandial glucose (PPG), lipid profiles, TG/HDL-C, TyG index, and Lp(a) in hy- pertensive patients with and without type 2 diabetes mellitus (T2DM).

Methods: A prospective cohort study was conducted from May to August 2025 at two centers in Karnataka, India, involving 300 hypertensive patients (150 diabetic, 150 non-diabetic). Participants received a Mediterranean diet, exercise, and optimized pharmacological therapy, with monthly monitoring of glycemic, homocysteine, and Lp(a) levels. Parameters were measured using standardized assays, and data were analyzed with SPSS v26.

Results: In diabetic patients, significant reductions were observed in HbA1c (8.1% to 7.2%, $p < 0.001$), PPG (180 to 145 mg/dL, $p < 0.001$), LDL-C (130 to 105 mg/dL, $p < 0.01$), homocysteine (15.2 to 12.8 μmol/L, $p < 0.01$), BMI (31.2 to 29.8 kg/m^2, $p < 0.01$), TG/HDL-C (4.2 to 3.5, $p < 0.01$), TyG index (8.9 to 8.4, $p < 0.01$), and Lp(a) (45 to 38 mg/dL, $p < 0.05$), with increased HDL-C (40 to 48 mg/dL, $p < 0.01$). Non-diabetic patients showed modest improvements in BMI, LDL-C, TG/HDL-C, and Lp(a) ($p < 0.05$). Strong correlations in diabetic patients were noted among homocysteine, BMI, HbA1c, TG/HDL-C, TyG index, and Lp(a) ($p < 0.01$). TyG index (cutoff 8.5) predicted CVD risk with 78% sensitivity and 65% specificity; Lp(a) (cutoff 30 mg/dL) offered 72% sensitivity and 68% specificity. Monthly moni- toring was cost-effective ($150/patient), potentially reducing CVD hospitalization costs ($10,000/event).

Conclusions: TG/HDL-C, TyG index, and Lp(a) are robust, cost-effective CVD risk markers. Integrated management of homocysteine, BMI, and Lp(a) enhances CVD prevention in high-risk populations.

Keywords: Cardiovascular Disease, Triglyceride-Glucose Index, TG/HDL-C Ratio, Lipoprotein(a), Homocysteine, Type 2 Diabetes, Hypertension

INTRODUCTION

Cardiovascular disease (CVD) accounts for 17.9 million deaths annually, driven by diabetic dyslipidemia, characterized by elevated triglycerides (TG), reduced high-density lipoprotein cholesterol (HDL-C), and increased

low-density lipopro- tein cholesterol (LDL-C) in type 2 diabetes mellitus (T2DM) patients (1; 2; 3). Poor glycemic control, marked by elevated HbA1c and postprandial glucose (PPG), ex- acerbates endothelial dysfunction (4). Hypertension amplifies atherosclerosis risk (5), while elevated homocysteine and lipoprotein(a) [Lp(a)] independently contribute to vascular damage and atherogenesis (6; 7; 8). The TG/HDL-C ratio and triglyceride-glucose (TyG) index are cost-effective markers of insulin resis- tance and CVD risk (9; 10). Intensive lifestyle and pharmacological interventions can improve cardio-metabolic profiles, reducing CVD events (11; 12).

This study investigates the interplay of homocysteine, BMI, HbA1c, PPG, lipid profiles, TG/HDL-C, TyG index, and Lp(a) in hypertensive patients with and with- out T2DM over a 3-month intervention, hypothesizing that integrated manage- ment enhances risk stratification and CVD prevention (13; 14).

Materials and Methods

Study Design

A prospective cohort study was conducted from May to August 2025 at Aski Super Specialty Hospital and Research Centre, Bagalkot, and MVJ Medical College and Research Hospital, Hoskote, Bangalore, Karnataka, India, involving 300 hyper- tensive patients (150 diabetic, 150 non-diabetic). Ethical approval was obtained (ASSH&RC/108/25-26, dated April 20, 2025).

Participants

Inclusion Criteria

- Age 40–79 years
- Hypertension (≥140/90 mmHg or on antihypertensive therapy) (15)
- Diabetic group: T2DM confirmed by HbA1c ≥6.5%, fasting plasma glucose (FPG) ≥7.0 mmol/L, or anti-diabetic medication (16)
- Willingness for monthly follow-ups

Exclusion Criteria

- Type 1 diabetes (17)
- Severe renal impairment (eGFR <15 mL/min/1.73 m^2) (18)
- Cardiovascular events within 6 months (19)
- Pregnancy, lactation, malignancy, or severe hepatic dysfunction (20)

Intervention

Participants received:

- **Lifestyle Modifications**: Mediterranean diet, 30 min moderate aerobic ex- ercise 4–6 times/week, 5–10% weight loss (21).
- **Pharmacological Therapy**: Optimized antihypertensive, anti-diabetic, and lipid-lowering therapies (15).
- **Monthly Monitoring**: HbA1c, FPG, PPG, homocysteine, and Lp(a) via stan- dardized assays (22).

Measurements

- **Glycemic**: HbA1c (high-performance liquid chromatography), FPG, PPG (enzymatic methods) (23; 24)
- **Lipid Profile**: TG, LDL-C, HDL-C (automated enzymatic assays), TG/HDL-C ratio (25)
- **TyG Index**: ln[TG (mg/dL) × FPG (mg/dL) / 2] (14)
- **Homocysteine**: Enzyme-linked immunosorbent assay (6)
- **Lipoprotein(a)**: Immunoturbidimetric assay (26)
- **Anthropometric**: BMI (kg/m^2), waist circumference, blood pressure (27)

Data Collection

Blood samples were collected post-12-hour fast; PPG measured 2 hours post- standardized meal. Assays were conducted at certified laboratories (28).

Statistical Analysis

Data were analyzed using SPSS v26. Normality was tested via Shapiro-Wilk. Con- tinuous variables were reported as means ± SD or medians (IQR). Spearman's correlations assessed relationships among homocysteine, BMI, HbA1c, PPG, TG/HDL- C, TyG index, and Lp(a). Paired t-tests or Wilcoxon signed-rank tests compared pre- and post-intervention parameters ($p < 0.05$) (29).

2 Results

2.1 Baseline Characteristics

Table 1 shows baseline characteristics. Diabetic patients (n=150, 52% male, 58.4 ± 8.7 years) had higher BMI (31.2 ± 4.5 kg/m^2), homocysteine (15.2 ± 3.1 μmol/L), HbA1c (8.1 ± 1.2%), TG/HDL-C (4.2 ± 1.1), TyG index (8.9 ± 0.7), and Lp(a) (45 ± 12 mg/dL) than non-diabetic patients (n=150, 48% male, 56.7 ± 9.1 years; BMI 29.8 ± 4.0 kg/m^2; homocysteine 12.5 ± 2.8 μmol/L; HbA1c 5.8 ± 0.4%; TG/HDL-C 3.1 ± 0.9; TyG index 8.2 ± 0.5; Lp(a) 32 ± 10 mg/dL).

Table 1: Baseline Characteristics of Study Participants

Parameter	Diabetic (n=150)	Non-Diabetic (n=150)	p-value
Age (years)	58.4 ± 8.7	56.7 ± 9.1	0.12
BMI (kg/m^2)	31.2 ± 4.5	29.8 ± 4.0	< 0.05
Homocysteine (μmol/L)	15.2 ± 3.1	12.5 ± 2.8	< 0.001
HbA1c (%)	8.1 ± 1.2	5.8 ± 0.4	< 0.001
FPG (mg/dL)	145 ± 30	95 ± 15	< 0.001
PPG (mg/dL)	180 ± 35	120 ± 20	< 0.001
LDL-C (mg/dL)	130 ± 25	125 ± 22	0.08
HDL-C (mg/dL)	40 ± 8	45 ± 7	< 0.01
TG/HDL-C Ratio	4.2 ± 1.1	3.1 ± 0.9	< 0.001
TyG Index	8.9 ± 0.7	8.2 ± 0.5	< 0.001
Lp(a) (mg/dL)	45 ± 12	32 ± 10	< 0.001

2.2 Intervention Outcomes

Table 2 summarizes changes post-intervention. Diabetic patients showed sig- nificant reductions in BMI (31.2 to 29.8 kg/m^2, $p < 0.01$), homocysteine (15.2 to 12.8 μmol/L, $p < 0.01$), HbA1c (8.1% to 7.2%, $p < 0.001$), PPG (180 to 145 mg/dL, $p < 0.001$), LDL-C (130 to 105 mg/dL, $p < 0.01$), TG/HDL-C (4.2 to 3.5, $p < 0.01$), TyG index (8.9 to 8.4, $p < 0.01$), and Lp(a) (45 to 38 mg/dL, $p < 0.05$), with increased HDL-C (40 to 48 mg/dL, $p < 0.01$). Non-diabetic patients showed modest reduc- tions in BMI (29.8 to 28.9 kg/m^2, $p < 0.05$), LDL-C (125 to 110 mg/dL, $p < 0.05$), TG/HDL-C (3.1 to 2.8, $p < 0.05$), and Lp(a) (32 to 29 mg/dL, $p < 0.05$).

2.3 Correlations

In diabetic patients, homocysteine correlated with HbA1c ($r = 0.48$, $p < 0.01$), TG/HDL-C ($r = 0.50$, $p < 0.01$), TyG index ($r = 0.52$, $p < 0.001$), and Lp(a) ($r = 0.45$, $p < 0.01$). BMI correlated with TG/HDL-C ($r = 0.46$, $p < 0.01$), TyG index ($r = 0.49$, $p < 0.01$), and Lp(a) ($r = 0.42$, $p < 0.01$). PPG correlated strongly with TG/HDL- C ($r = 0.55$, $p < 0.001$) and Lp(a) ($r = 0.47$, $p < 0.01$). In non-diabetic patients, correlations were weaker (homocysteine vs. TG/HDL-C: $r = 0.28$, $p < 0.05$; BMI vs. TyG index: $r = 0.30$, $p < 0.05$; Lp(a) vs. TG/HDL-C: $r = 0.25$, $p < 0.05$).

Table 2: Pre- and Post-Intervention Changes in Key Parameters

Parameter	Group	Pre-Intervention	Post-Intervention	p-value
BMI (kg/m^2)	Diabetic	31.2 ±4.5	29.8 ±4.3	< 0.01
Non-Diabetic		29.8 ±4.0	28.9 ±3.8	< 0.05
Homocysteine (μmol/L)	Diabetic	15.2 ±3.1	12.8 ±2.9	< 0.01
Non-Diabetic		12.5 ±2.8	11.9 ±2.7	0.08
HbA1c (%)	Diabetic	8.1 ±1.2	7.2 ±1.0	< 0.001
Non-Diabetic		5.8 ±0.4	5.7 ±0.4	0.12
PPG (mg/dL)	Diabetic	180 ±35	145 ±30	< 0.001
Non-Diabetic		120 ±20	115 ±18	0.09
LDL-C (mg/dL)	Diabetic	130 ±25	105 ±20	< 0.01
Non-Diabetic		125 ±22	110 ±20	< 0.05
HDL-C (mg/dL)	Diabetic	40 ±8	48 ±9	< 0.01
Non-Diabetic		45 ±7	47 ±7	0.07
TG/HDL-C Ratio	Diabetic	4.2 ±1.1	3.5 ±1.0	< 0.01
Non-Diabetic		3.1 ±0.9	2.8 ±0.8	< 0.05
TyG Index	Diabetic	8.9 ±0.7	8.4 ±0.6	< 0.01
Non-Diabetic		8.2 ±0.5	8.0 ±0.5	0.06
Lp(a) (mg/dL)	Diabetic	45 ±12	38 ±11	< 0.05
Non-Diabetic		32 ±10	29 ±9	< 0.05

2.4 Diagnostic Markers

The TyG index was higher in diabetic patients (8.9 vs. 8.2, $p < 0.001$) and de- creased post-intervention ($p < 0.01$), with a cutoff of 8.5 predicting CVD risk (78% sensitivity, 65% specificity) (30). Lp(a) was elevated in diabetic patients (45 vs. 32 mg/dL, $p < 0.001$) and decreased post-intervention ($p < 0.05$), with a cutoff of 30 mg/dL predicting CVD risk (72% sensitivity, 68% specificity) (31).

2.5 Cost-Effectiveness

Monthly monitoring cost $150/patient over 3 months, enabling early detection of glycemic, homocysteine, and Lp(a) excursions, potentially reducing CVD hos- pitalization costs ($10,000/event) (32).

3 Discussion

This study demonstrates significant interrelationships among homocysteine, BMI, glycemic control, dyslipidemia, and Lp(a) in diabetic hypertensive patients, align- ing with prior evidence linking these factors to CVD risk (33; 34). Elevated homo- cysteine, BMI, and Lp(a) correlated strongly with TG/HDL-C and TyG index in dia- betic patients ($p < 0.01$), reflecting their roles in endothelial dysfunction, insulin resistance, and atherogenesis (6; 7; 8). The 3-month intervention significantly improved BMI, homocysteine, HbA1c, PPG, LDL-C, HDL-C, TG/HDL-C, TyG index,

and Lp(a) in diabetic patients, supporting the efficacy of combined lifestyle and pharmacological strategies (35; 36). Non-diabetic patients showed modest im- provements, likely due to lower baseline risk.

The inclusion of Lp(a), a genetically influenced CVD risk marker, enhances the study's novelty by demonstrating its responsiveness to intervention and cor- relation with insulin resistance markers (8). TG/HDL-C, TyG index, and Lp(a) emerged as cost-effective tools for CVD risk assessment, suitable for clinical inte- gration (37; 38). Monthly monitoring facilitated timely interventions, supporting scalability in resource-limited settings (39).

Limitations: The 3-month duration limits long-term outcome assessment. The lack of a control group restricts causal inference. The cohort, limited to two centers in Karnataka, may not reflect broader populations due to regional ge- netic and dietary variations. Lp(a) assay variability and unexamined genetic influences are additional constraints (26). Future studies should include longer follow-ups, control groups, diverse cohorts, and genetic analyses to validate these markers for CVD risk stratification (40). Regional cost variations also require fur- ther exploration (41).

4 Conclusions

- A 3-month lifestyle and pharmacological intervention significantly improves glycemic, lipid, homocysteine, BMI, and Lp(a) profiles in diabetic hyperten- sive patients, reducing CVD risk.
- TG/HDL-C, TyG index, and Lp(a) are effective, cost-effective CVD risk mark- ers.
- Monthly monitoring of glycemic, homocysteine, and Lp(a) levels is cost- effective and supports early intervention.
- Integrated management of homocysteine, BMI, and Lp(a) enhances person- alized CVD prevention.

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6 Author Contributions

- Dr,**Preeti V. Aski:** Conceptualized the study, recruited subjects, collected data, performed clinical assessments, conducted literature review, curated data, validated results, drafted the manuscript.
- Dr,**Nikhil S. Aski:** Performed statistical analysis, created data visualizations, interpreted results, prepared tables (including Lp(a) correlations).
- Dr.**Nikil N. Biradar:** Assisted in laboratory analyses (including Lp(a) estimation), managed sample processing, contributed to data organization, and supported manuscript preparation.
- Dr.**Busi Karunanand:** Reviewed the manuscript, provided critical revisions, and supported editing.
- Dr.**Basavaraj S. Aski:** Designed the study, supervised the research, obtained ethical clearance, coordinated the project, and approved the final manuscript.

7 Funding

This research received no external funding.

8 Conflicts of Interest

The authors declare no conflicts of interest.

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