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# Diagnostic value of postprandial triglycerides testing in diabetic patients: Case series

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## Abstract

Postprandial hypertriglyceridemia is now established as an important risk factor for cardiovascular disease (CVD). This metabolic abnormality is principally initiated by overproduction and/or decreased catabolism of triglyceride-rich lipoproteins (TRLs) and is a consequence of predisposing genetic variations and medical conditions such as obesity and insulin resistance. Accumulation of TRLs in the postprandial state promotes the retention of remnant particles in the artery wall. Because of their size, most remnant particles cannot cross the endothelium as efficiently as smaller low-density lipoprotein (LDL) particles. However, since each remnant particle contains approximately 40 times more cholesterol compared with LDL, elevated levels of remnants may lead to accelerated atherosclerosis and CVD. The recognition of postprandial hypertriglyceridemia in the clinical setting has been severely hampered by technical difficulties and the lack of established clinical protocols for investigating postprandial lipemia, The aim of our study is to evaluate the diagnostic value of postprandial triglycerides (TG) in type 2 diabetic subjects.

**Patients and Methods**: This was a prospective, descriptive, cross-sectional study of 112 patients diabetes, from April 2022 to July 2022.

**Results:** Our population consisted of 112 diabetic patients aged between 30 and 70 years, with an average age of 50. Taking into account the established thresholds: A normal postprandial triglyceride level is defined as a serum level of of 1.82±0.40 at 2h, our study shows a prevalence of post prandial hypertriglyceridaemia of 52%.

**Conclusion:** The findings of this study indicate that patients with type 2 diabetes who were subjected to a standardised fat meal challenge exhibited a notable elevation in triglyceride levels following the ingestion of the meal. It can be postulated that persistent postprandial hypertriglyceridemia may result in a pro-atherogenic environment, which in turn may lead to the development of atherosclerosis and macrovascular disease in subjects with type 2 diabetes.

**Keywords:** Post prandial hypertriglyceridemia; Diabetes; Cardiovascular disease

## 1. Introduction

Dyslipidemia that accompanies type 2 diabetes plays an important role in the pathogenesis of accelerated atherosclerosis in this population[1,2]The most important components of this dyslipidemia are an elevated very low density lipoproteins (VLDL) and total triglycerides (TGs) and a decreased high density lipoproteins (HDL) concentration in the serum. [3] While fasting hypertriglyceridemia may be a risk factor for atherosclerosis, particularly in the presence of diabetes mellitus[2,3] this association has not been consistent and fasting HDL-C appears to be a far more significant risk factor[4,5] However, when TGs are studied in postprandial state, they emerge as stronger and independent coronary risk factors than HDL-C. [6,7] Postprandial hypertriglyceridemia have been linked with asymptomatic and symptomatic macrovascular disease in both normo-and hypertriglyceridemic subjects [8,9] and such abnormalities have been reported in type 2 diabetics ,the increased risk of atherosclerosis among them, might therefore be related to

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the higher postprandial lipemia in them. Earlier studies from our institution clearly demonstrate the presence of postprandial hypertriglyceridemia among diabetic subjects, irrespective of fasting triglyceride levels [10].

## 2. Patients and Methods

This was a prospective, descriptive, cross-sectional study of 112 patients. spread over a period of 4 months (April 2022 to July 2022) all patients included in our study followed in the endocrinology department of the Avicenne military Avicenne military hospital in Marrakech

Investigations according to standardized methods were carried out by screening teams . All invited persons were asked to fill in the main questionnaire and bring it to the screening station. Then, according to the protocol, a trained nurse checked it for omissions and inconsistencies. The questionnaire covered among other things, age gender history of previous cardiovascular disease and disease symptoms, current medication, level of leisure time physical activity, and smoking habits. Menopause was registered by personal interview. Moreover, a simple clinical examination was performed. Body weight (kilograms) and height (cm) were measured with the participants wearing light clothing without shoes. Body mass index (BMI) was computed as weight/height$^2$ (kg/m$^2$).

Each patient received, upon admission, a sample of five millilitres of whole blood on a dry tube, centrifuged at 3000 rpm for five minutes. The biochemical parameters were determined by chemiluminescence method using the Cobas Roche multiparametric analyzer.

All the patients underwent a biochemical indexes: fasting and postprandial glycemia , postprandial triglycerides

## 3. Results

The median age in patients was 50 (30-70 years), the 30-50 years age group accounted for 65% of patients. Women represented 65% of the study population. Most patients had one or more co-morbidities, hypertension and diabetes mellitus was the commonest of comorbidities (table 1)

**Table 1** Number of comorbidities per patient

| **Characteristics** | **Total (N=112)** |
|---|---|
| Median age | 50 |
| Female | 58 |
| male | 54 |
| Diabetes | 112 (100%) |
| Hypertension | 76 (85%) |
| Renal failure | 18(20%) |
| Others | 10(9%) |

Our study shows a prevalence of postprandial hypertriglyceridemia of 52%. Men had lower levels of triglycerides compared to women, medians (range) triglycerides were 2.05 mmol/l and 2.45 mmol/l, respectively. Mean age, total cholesterol, systolic and diastolic blood pressure, BMI, the proportions of smokers and physically inactive individuals increased over the quintiles for both women and men. The proportion of post-menopausal women also increased with increasing quintiles of triglycerides.

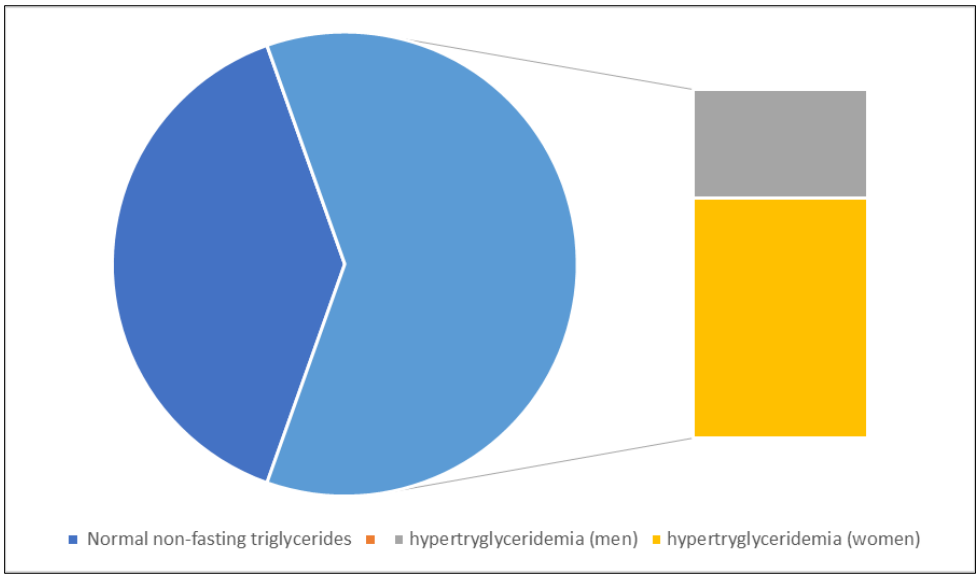


**Figure 1** Prevalence of hypertriglyceridemia stratified by gender

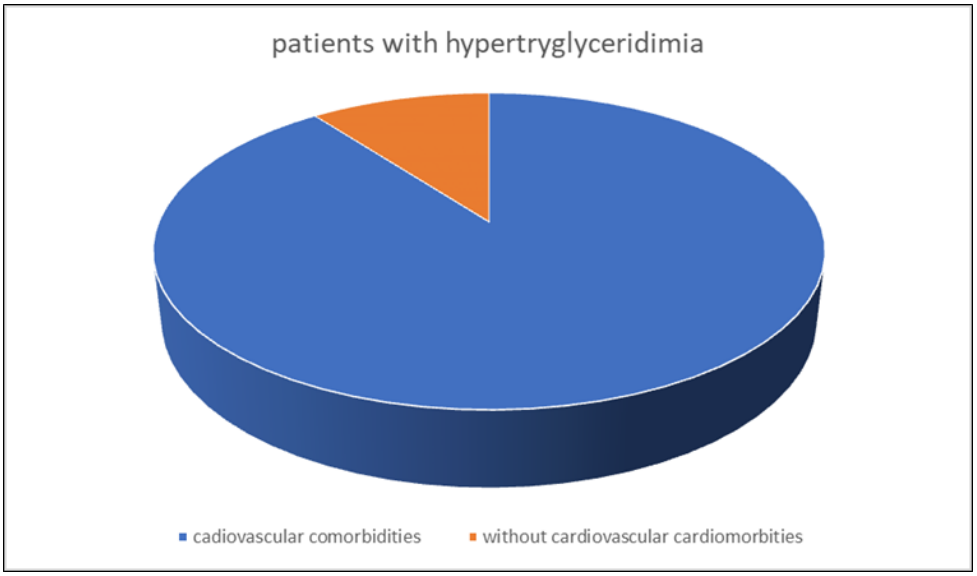


**Figure 2** Prevalence of Selected Cardiovascular and Non-Cardiovascular Comorbidities among Patients

## 4. Discussion

Subjects with diabetes have an increased risk of cardiovascular disease compared to a non-diabetic population [11]. Conventional risk factors, such as elevated serum total and low density lipoprotein (LDL) cholesterol, low high density lipoprotein (HDL) cholesterol, and hypertension, explain only part of this excess risk [11]. Core elements of dyslipidemia in type 2 diabetes are mild to moderate hypertriglyceridemia, low HDL cholesterol, and preponderance of small, dense LDL particles. All these features are believed to increase the risk of cardiovascular complications [12,13]. In the postprandial period, diabetic subjects have exaggerated hyperglycemia and hypertriglyceridemia. The postprandial lipemia consists of triglyceride-rich lipoproteins (TRL) including chylomicrons and their remnants derived from intestine and hepatic released very low-density lipoprotein (VLDL) particles. Chylomicrons and VLDL particles compete for the same catabolic pathways that include lipolysis by lipoprotein lipase (LPL) and hepatic lipase (HL) and direct uptake of TRL by the liver. Consequently, conditions in which VLDL production is high favour the accumulation of postprandial TRL. Acute hyperinsulinemia suppresses the production of large triglyceride-rich VLDL1 particles (Sf 60–400) in the liver in healthy men, but this downregulation of VLDL1 production by insulin is defective in subjects with

type 2 diabetes [14]. Accordingly, the inappropriate release of large VLDL1 particles in the postprandial phase is likely to be a contributing factor to hypertriglyceridemia. Growing evidence suggests that TRL and their remnants are atherogenic, possibly owing to their direct effects on the vascular wall or owing to the secondary effects of TRL on HDL and LDL particles [15–16]. A number of cross-sectional and prospective studies have associated small, dense LDL particles with cardiovascular disease [13,17,18]. However, because of the close correlations between small, dense LDL, hypertriglyceridemia, and low HDL cholesterol [19], it is difficult to dissect out whether small LDL particles are an independent risk factor or are merely a marker of other factors with causal relationship to atherosclerosis.

| Study [ref.] | Population | Follow-up | Main outcomes | Remarks |
|---|---|---|---|---|
| Norwegian counties study [111] | 43,641 men and 42, 600 women free of CVD | Prospective, 27 years | HRs (95%CI) per 1 mmol/L increase in non-fasting TGs for all causes, CVD, IHD, and stroke mortality:<br>Women: 1.16 (1.13–1.20), 1.20 (1.14–1.27), 1.26 (1.19–1.34) and 1.09 (0.96–1.23)<br>Men: 1.03 (1.01–1.04), 1.03 (1.00–1.05), 1.03 (1.00–1.06) and 0.99 (0.92–1.07). | Adjustment for major cardiovascular risk factors attenuated the effect |
| Copenhagen City Heart study [2,112] | Random population sample of 6391 men and 7581 women | Prospective, 31 years | HRs (95%CI) for total mortality by non-fasting TGs:<br>(TG < 1 mmol/L: HR 1)<br>TG 1.0–1.99 mmol/L: 1.1 (95%CI: 1.0–1.2) in women and 1.1 (95%CI: 1.1–1.2) in men<br>TG 2.0–2.99 mmol/L: 1.3 (95%CI: 1.2–1.4) in women and 1.2 (95%CI: 1.1–1.4) in men<br>TG 3.0–3.99 mmol/L: 1.4 (95%CI: 1.2–1.7) in women and 1.3 (95%CI: 1.1–1.4) in men<br>TG 4.0–4.99 mmol/L: 1.4 (95%CI: 1.1–1.9) in women and 1.4 (95%CI: 1.2–1.6) in men<br>TG > 5 mmol/L: 2.0 (95%CI: 1.5–2.7) in women and 1.5 (95%CI: 1.2–1.7) in men | The best predictor for MI in women was non-fasting TG and in men non-fasting cholesterol |
| Copenhagen City Heart study [113] | Random population sample of 6372 men and 7579 women | Prospective, 33 years | HRs (95%CI) for ischemic stroke by non-fasting TGs:<br>(TG < 1 mmol/L: HR 1)<br>TG 1.0–1.99 mmol/L: 1.2 (95%CI: 0.9–1.7) in women and 1.2 (95%CI: 0.8–1.7) in men<br>TG > 5 mmol/L: 3.9 (95%CI: 1.3–11.1) in women and 2.3 (95%CI: 1.2–4.3) in men | The remnant cholesterol increased stepwise as a function of non-fasting TG and cholesterol in cross-sectional analysis of 53,629 subjects (see also Fig. 1.) |
| The Women's Health study [3] | 26,509 initially healthy US women of which 6391 had non-fasting samples | Prospective, 11 years | HR for CVD event by non-fasting TG:<br>2nd tertile: 1.44 (95% CI 0.90–2.29)<br>3rd tertile: 1.98 (95% CI 1.21–3.25) | TG measured 2 to 4 h postprandially had the strongest association with CVD events (fully adjusted HR [95% CI] for highest vs. lowest tertiles of levels, 4.48 [1.98–10.15] [P < .001 for trend]) |
| The Framingham study [117] | 1567 women offspring of the original Framingham cohort: 83 with and 1484 without CVD | Cross-sectional | RLP-chol + 15.6%; P < 0.0001 and RLP-TG + 27.0%; P < 0.0002 in women with prevalent CVD | Adjusted RLP-chol was significantly associated with prevalent CVD in women in logistic regression analysis |
| Kugiyama et al. [118] | 147 consecutive patients with CAD | Prospective follow-up until coronary event or 36 months | OR for developing coronary event:<br>2nd tertile of remnant levels 2.43 (95%CI: 1.1–5.8)<br>3rd tertile of remnant levels 6.38 (95%CI:2.3–17.6) | Remnant levels were independent predictors of future coronary event in multivariate model |
| The Honolulu Heart study [119] | 1156 Japanese-American men | Prospective, 17 years | RLP-chol (P = 0.0022) and RLP-TG (P = 0.0045) predicted CHD risk independent of non-lipid risk factors | RLP-chol and RLP-TG were only significant lipid predictors of CHD in models with total, HDL and LDL cholesterols as additional covariates |

**Figure 3** Epidemiologic studies reporting non-fasting triglycerides (TG) or remnant lipoproteins and the risk for cardiovascular morbidity and mortality

Hypertriglyceridemia is considered as the primary abnormality of the dyslipidemia associated with T2DM. In a large population based study of patients with T2DM in Sweden, about 37% had moderately elevated triglycerides (>1.7 mmol/L or >150 mg/dL) and 3.4% had pronounced hypertriglyceridemia (>4.0 mmol/l or >356 mg/dL) [20]. Hypertriglyceridemia is often accompanied by low levels of HDL cholesterol because of the transfer of triglycerides from TRLs to HDL particles by cholesteryl ester transfer protein (CETP) and rapid catabolism of the triglyceride enriched HDL particles by hepatic lipase . Likewise, transfer of triglycerides from TRLs to LDL particles by CETP and increased lipolysis of triglyceride-rich LDL results in sdLDL particles (Figure 1) [21]. Increased production of large triglyceride-rich apoB100- containing VLDL particles called VLDL1 in the liver is the major determinant of raised triglyceride levels in individuals with T2DM along with disturbances of apoCIII metabolism . In addition, elevated plasma concentrations of intestinal apoB48-containing CM and CM remnant particles occur in insulin resistant states and contribute to the postprandial hyperlipidemia [22]. The production of intestinal lipoproteins is related to the amount of fat ingested and absorbed, but in insulin resistance and T2DM there is chronic overproduction of intestinal apoB48-containing lipoproteins [23]. It was recognized in the 1970s that apoB48- and apoB100- containing particles are cleared from the circulation by common, saturable pathways and consequently compete for clearance [24]. Therefore, increased secretion of VLDL from the liver is an important determinant of postprandial accumulation of CMs and CM remnants. Whilst over 80% of the increase in triglycerides after a fat rich meal comes from apoB48-containing lipoproteins [25], the smaller apoB100 -containing VLDL particles account for about 80% of the increase in particle number [26]. The dyslipidemia in T2DM is not only related to macrovascular disease but is also associated with microvascular diabetic kidney disease. A case-control study in 13 countries found that diabetic kidney disease was associated with higher plasma triglyceride levels and lower levels of HDL cholesterol among patients with good control of LDL cholesterol, but diabetic retinopathy was less robustly associated with these lipids [27].

In recent years, the recognition of biological pathways, Mendelian randomization studies and large epidemiologic findings support strong links between remnant cholesterol and atherosclerosis [28].

## 5. Conclusion

In conclusion, our findings indicate a stronger correlation between non-fasting triglycerides and the risk of developing cardiovascular disease. However, the advent of novel therapeutic approaches utilizing anti-sense oligonucleotides or siRNA to target regulatory genes involved in postprandial lipid metabolism offers a promising avenue for future management strategies.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclsoed.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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