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Exploring the Role of Triglycerides in Diabetes: Implications for Clinical Practice and Therapeutic Approaches

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***Abstract*: Triglycerides (TG) have an important role in the pathophysiology of diabetes Mellitus, especially in the initial stage and well as its management. This narrative review explores the complicated relationship between TG levels in the body and diabetes management, its biochemical importance, metabolic pathways and its clinical impacts on the human body. As per the available literature, we would like to give detailed information about the effect of TG on diabetes and a more detailed treatment strategy based on their levels in the blood.**

***Keywords*: Diabetes Mellitus, Metabolic Pathways, Management strategies, Pathophysiology, TG.**

1. Introduction

TG (TG) are the common form of fat present in the human body and are also known as an important energy resource. Increased TG is related to metabolic abnormalities, especially diabetes. Some of the other factors related to diabetes are style, hereditary, climatic factors etc. The interconnect between diabetes and TG is complicated and it consists of various metabolic pathways and regulatory mechanisms. This review aims to elaborate on the relationships between TG and diabetes and provide insights into potential therapeutic targets for improving diabetes outcomes [1].

A. Biochemistry of TG

TG are made of three fatty acids esterified to form glycerol molecules. They are stored in adipose tissue and whenever in require of energy, that is used. Production and destruction of TG is the synthesis and breakdown of TG are tightly regulated by hormonal signals, primarily insulin, which promotes TG storage, and glucagon, which stimulates TG breakdown [2].

B. TG and Diabetes Pathology

Those with diabetes especially type 2 diabetes mellitus(T2DM), usually present with Hypertriglyceridemia. Insulin resistance is the main pathophysiology behind this and it will lead to altered lipid metabolism. insulin resistance impairs the inhibitory effect of insulin on hormone-sensitive lipase in adipose tissue. This will lead to elevated TG hydrolysis and free fatty acids release. These free fatty acids will reach the liver and promote hepatic TG synthesis and very low-density lipoprotein (VLDL) production [3].

C. Food Sources that Increase TG

Elevated TG levels can be influenced significantly by dietary choices. Certain foods can increase TG levels due to their composition and the metabolic responses they trigger. Understanding which foods contribute to higher TG can help individuals manage their levels through dietary modifications. Here are the main food sources that are known to increase TG [4]-[6].

2. Sugary Foods and Beverages

Beverages like sodas, sweetened fruit juices, and energy drinks contain high amounts of added sugars, which can elevate TG levels. Pastries, cakes, candies, and other sugary treats can increase TG due to their high sugar content.

A. Refined Carbohydrates

Foods made from refined flour, such as white bread, pasta, and white rice, can cause spikes in blood sugar and, consequently, TG levels. Crackers, chips, and other processed snacks often contain refined carbohydrates and added sugars.

B. Alcohol

Alcohol can increase TG levels, especially when consumed in excess. Beverages like beer, wine, and spirits contribute to elevated TG and should be consumed in moderation.

1) High-Fat Foods

Foods that are deep-fried, such as French fries, fried chicken, and doughnuts, contain high levels of unhealthy fats, which can raise TG. Many fast food items are high in unhealthy fats and refined carbohydrates, both of which can increase TG levels.

2) Trans Fats

Foods containing partially hydrogenated oils, such as some margarine, baked goods, and processed foods, are high in trans fats, significantly raising TG levels. Items like cookies, cakes, and pies often contain trans fats.

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Table 1
Dietary Management, TG and Effect on Diabetes [4]–[7]

Dietary Component	Effect on TG	Impact on Diabetes Management
Refined Carbohydrates and Sugars	Increase TG by causing rapid blood sugar spikes	Poor glycemic control and increased cardiovascular risk
Omega-3 Fatty Acids	Lower TG by reducing hepatic synthesis and increasing clearance	Improved lipid profile and reduced cardiovascular risk
Fiber-Rich Foods	Lower TG by slowing sugar and fat absorption	Better glycemic control and reduced cardiovascular risk
Healthy Fats (Monounsaturated and Polyunsaturated)	Lower TG by replacing saturated and trans fats	Improved lipid profile and enhanced insulin sensitivity
Alcohol	Raises TG, especially in predisposed individuals	Increased cardiovascular risk and potential complications in diabetes management
Weight Management	Reduces TG by promoting overall metabolic health	Improved insulin sensitivity, better glycemic control, and reduced cardiovascular risk

3) High-Saturated Fat Foods

Red meats with visible fat, such as beef, pork, and lamb, contain high levels of saturated fats. Full-fat dairy products, such as whole milk, cheese, butter, and cream, contribute to higher TG levels.

4) Processed and Packaged Foods

Many frozen and canned meals are high in unhealthy fats, sugars, and refined carbohydrates. Packaged snacks like potato chips, pretzels, and snack bars often contain high levels of sugar, fats, and refined carbs.

5) High-Calorie Foods

Consuming large portions of food, regardless of the type, can lead to increased TG levels, as the body stores excess calories as fat.

3. Foods for High and Low TG High TG

A. Foods To Avoid High TG

1) Refined Carbohydrates and Sugars

Foods such as white bread, pastries, sugary drinks, and candies can raise TG levels. These foods cause rapid spikes in blood sugar, leading to increased insulin production and subsequent TG synthesis.

2) Saturated and Trans Fats

Red meats, full-fat dairy products, fried foods, and processed snacks contain high levels of these fats, which can elevate TG levels and contribute to cardiovascular diseases.

Alcohol: Excessive alcohol consumption can significantly raise TG levels, particularly in individuals with a predisposition to high TG.

B. Foods to Include

1) Omega-3 Fatty Acids

Found in fatty fish (salmon, mackerel, sardines), flaxseeds, chia seeds, and walnuts, these fats help lower TG levels by reducing the rate of hepatic TG synthesis and increasing the clearance of TG-rich lipoproteins.

2) Fiber-Rich Foods

Whole grains, legumes, fruits, and vegetables are high in fibre, which helps reduce TG levels by slowing the absorption of sugar and fat in the digestive tract.

3) Healthy Fats

Avocado, olive oil, and nuts provide monounsaturated and polyunsaturated fats, which can lower TG and improve overall lipid profiles.

C. Foods to Avoid for Low TG

Refined Carbohydrates and Sugars: Even with low TG levels, it is essential to avoid excessive refined sugars and carbohydrates to maintain overall health and prevent future lipid imbalances.

1) Trans Fats

Processed and fried foods should be avoided to prevent potential increases in TG and other lipid abnormalities.

D. Foods to Include

Balanced Diet: A diet that includes a variety of fruits, vegetables, whole grains, lean proteins, and healthy fats supports overall lipid health and maintains low TG levels.

Lean Proteins: Skinless poultry, fish, beans, and legumes provide necessary protein without contributing to high TG levels.

4. Clinical Implications of Hypertriglyceridemia in Diabetes

1. *Cardiovascular Risk*: Hypertriglyceridemia is a significant risk factor for cardiovascular disease (CVD), which is the leading cause of morbidity and mortality in diabetic patients. Elevated TG levels contribute to atherogenic dyslipidemia, characterized by high levels of small, dense low-density lipoprotein (LDL) particles and low levels of high-density lipoprotein (HDL) cholesterol.
2. *Pancreatitis*: Severe hypertriglyceridemia can lead to acute pancreatitis, a potentially life-threatening condition. Diabetic patients with poorly controlled hyperglycemia and high TG levels are particularly susceptible.
3. *Glycemic Control*: Elevated TG can interfere with glucose metabolism, exacerbating insulin resistance and impairing glycemic control. This creates a vicious cycle, as poor glycemic control further worsens lipid abnormalities [8]-[12].

5. Therapeutic Approaches

Effective management of Hypertriglyceridemia in diabetic patients involves lifestyle interventions, pharmacotherapy, and, in some cases, surgical options.

A. Lifestyle Interventions

Dietary modifications, including reduced intake of simple sugars and saturated fats, increased consumption of omega-3 fatty acids, and regular physical activity, are foundational. Weight loss through calorie restriction and exercise improves insulin sensitivity and lowers TG levels [13].

B. Pharmacotherapy

1) Fibrates

Fibrates, such as fenofibrate and gemfibrozil, are the primary agents for reducing TG levels. They activate peroxisome proliferator-activated receptor-alpha (PPAR-α), enhancing TG clearance [14].

2) Omega-3 Fatty Acids

High-dose omega-3 fatty acids (eicosapentaenoic acid and docosahexaenoic acid) reduce TG synthesis and increase clearance.

3) Statins

While primarily used for lowering LDL cholesterol, statins also have modest TG-lowering effects.

4) Niacin

Niacin reduces TG synthesis and VLDL secretion but is limited by side effects such as flushing and potential worsening of glycemic control.

5) Novel Agents

Emerging therapies targeting apolipoprotein C-III and angiopoietin-like protein 3 show promise in reducing TG levels [15].

C. Surgical Options

Bariatric surgery, particularly gastric bypass, can significantly reduce TG levels and improve glycemic control in obese diabetic patients.

6. Mechanism Behind the TG-Induced Insulin Resistance

Several mechanisms have been proposed to explain how elevated TG contribute to insulin resistance [16].

1. *Ectopic Fat Deposition*: Excess TG is deposited in non-adipose tissues, such as the liver and muscle, impairing insulin signalling pathways.
2. *Lipotoxicity:* Accumulation of toxic lipid intermediates, such as diacylglycerol and ceramides, interferes with insulin receptor signalling.
3. *Inflammation:* Hypertriglyceridemia induces a pro-inflammatory state, further exacerbating insulin resistance through cytokine-mediated pathways.

7. Role of TG in Beta-Cell Dysfunction

Beta-cell dysfunction is a critical factor in the progression of diabetes. Elevated TG levels can impair beta-cell function through

1. *Lipotoxicity:* Excess fatty acids and TG accumulate in pancreatic beta cells, causing cellular dysfunction and apoptosis.
2. *Oxidative Stress:* Hypertriglyceridemia induces oxidative stress in beta cells, leading to impaired insulin secretion.
3. *ER Stress:* Elevated TG disrupt endoplasmic reticulum (ER) homeostasis in beta cells, impairing insulin synthesis and secretion.

8. Impact of Glycemic Control on TG Levels

Effective glycemic control is essential for managing Hypertriglyceridemia. Improved glycemic control reduces TG levels through [17], [18]:

1. *Insulin Therapy:* Insulin therapy enhances TG clearance by upregulating lipoprotein lipase activity and reducing hepatic VLDL production.
2. *Oral Hypoglycemic Agents*: Medications such as metformin and thiazolidinediones improve insulin sensitivity, leading to lower TG levels.
3. *Incretin-Based Therapies:* GLP-1 receptor agonists and DPP-4 inhibitors improve postprandial lipid metabolism, reducing TG levels.

9. Emerging Therapies Targeting TG

Several novel therapeutic approaches are being explored to specifically target Hypertriglyceridemia in diabetic patients:

1. *Gene Therapy:* Gene editing technologies, such as CRISPR/Cas9, hold potential for correcting genetic mutations associated with Hypertriglyceridemia.
2. *Apolipoprotein C-III Inhibitors:* Apolipoprotein C-III plays a critical role in TG metabolism. Inhibitors of this protein show promise in reducing TG levels.
3. *Angiopoietin-Like Protein 3 Inhibitors:* Angiopoietin-like protein 3 regulates TG metabolism, and its inhibition leads to significant TG reduction.

10. Conclusion

TG have a profound impact on diabetes management, influencing both the pathophysiology and clinical outcomes of the disease. Effective management of Hypertriglyceridemia is crucial for reducing cardiovascular risk, preventing pancreatitis, and improving glycemic control. A multifaceted approach involving lifestyle modifications, pharmacotherapy, and novel therapeutic strategies is essential for optimal diabetes care. Continued research into the mechanisms underlying TG-induced insulin resistance and beta-cell dysfunction will provide further insights into potential therapeutic targets, enhancing the management of diabetes and its complications.

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Conflict of Interest

There is no conflict of interest by any of the authors.

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