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Letter to Editor

Severe Hypertriglyceridemia Managed Successfully in Primary care: A Pragmatic Clinical Observation

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Dear Editor,

Hypertriglyceridemia is defined by the National Cholesterol Education Program Adult Treatment Panel III as fasting blood plasma triglyceride (TG) levels ≥150 mg/dL. Various societies have given different classification of hypertriglyceridemia. Plasma TG level between 150 and 499 mg/dL are considered borderline to high, levels ≥ 500 mg/dL are classified as very high [1]. A subset of patients may develop "very severe hypertriglyceridemia," which the Endocrine Society defines as a serum triglyceride concentration ≥2000 mg/dL [2]. TG levels exceeding 1,000 mg/dL are associated with increased risk of acute pancreatitis. Apart from this triglyceride-rich lipoproteins and elevated triglyceride levels are recognized as independent contributors to atherosclerotic cardiovascular disease, emphasizing the need for targeted management [3].

The etiology of very severe hypertriglyceridemia may be either primary (genetic) or secondary. Primary causes include biallelic mutations affecting Lipoprotein lipase (*LPL),* apolipoprotein C2 (*APOC2*), lipase maturation factor 1 (*LMF1*), apolipoprotein 5 (*APOA5*), and glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein 1 (*GPIHBP1*). Patients with familial chylomicronemia syndrome or type 1 hyperlipoproteinemia typically harbor pathogenic mutations in these genes and often present at a younger age with recurrent acute pancreatitis. There are numerous etiologies of secondary hypertriglyceridemia that are more common and include uncontrolled diabetes mellitus, nephrotic syndrome, excessive alcohol use, and the use of certain medications such as protease inhibitors,

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vitamin A derivatives, l-asparaginase, and estrogen. Additional contributory factures include obesity, metabolic syndrome, chronic kidney disease, hypothyroidism, betablockers, thiazide diuretics, and estrogen containing preparations, cigarette smoking, high carbohydrate diet (>60% of energy intake) which are frequently encountered in routine clinical practice [2].

Clinically, hypertriglyceridemia may remain asymptomatic or present with eruptive xanthomas, lipemia retinalis, hepatosplenomegaly, and lipemic plasma (Figure 1). Severe hypertriglyceridemia is a well- recognized to be a risk factor for acute pancreatitis, particularly when TG levels exceed 1,000 mg/dL. Pancreatitis may be complicated by systemic inflammatory response, multiorgan failure, pancreatic necrosis and mortality as high as 20%. This risk can be reduced by lowering serum triglyceride levels below 1000mg/dL through correction of underlying causes, adherence to a low-fat diet, and pharmacotherapy [4-6]. Very severe hypertriglyceridemia warrants inpatient management with insulin infusion to reduce the risk of acute pancreatitis. Insulin accelerates triglyceride clearance by enhancing lipoprotein lipase activity [7]. Plasma exchange has been utilized in management of hypertriglyceridemia causing severe pancreatitis [8].

Emerging therapies for triglyceride lowering, including apoC-III inhibitors (volanesorsen, olezarsen) and ANGPTL3 inhibitors (evinacumab, vupanorsen) have shown marked reduction in TG levels and potential reduction in risk of pancreatitis in patients with severe or familial hypertriglyceridemia [9]. While most of these are still in research, prescription of these drugs available for clinical use remains limited by availability and cost in routine primary care practice in third world countries.

We share a clinical observation that highlights the challenges and outcomes of managing very severe hypertriglyceridemia in a primary care setting when referral for inpatient care is declined.

A 45-year-old male presented to primary care clinic with newly diagnosed Type 2 Diabetes mellitus and markedly elevated serum triglycerides (4241mg/dL). The abnormal lipid profile was detected during initial metabolic evaluation. He had no prior history of dyslipidemia or pancreatitis. General and systemic examination were unremarkable. There were no any clinical or biochemical evidence suggestive of acute pancreatitis. His blood sample was lipemic (Figure 1). In view of severe high TG levels and the associated risk of acute pancreatitis, the patient was strongly advised for referral to tertiary care for inpatient management. Patient was adequately counselled regarding risks associated with very severe Hypertriglyceridemia. However, citing various constrains, the patient declined referral and hospitalization.

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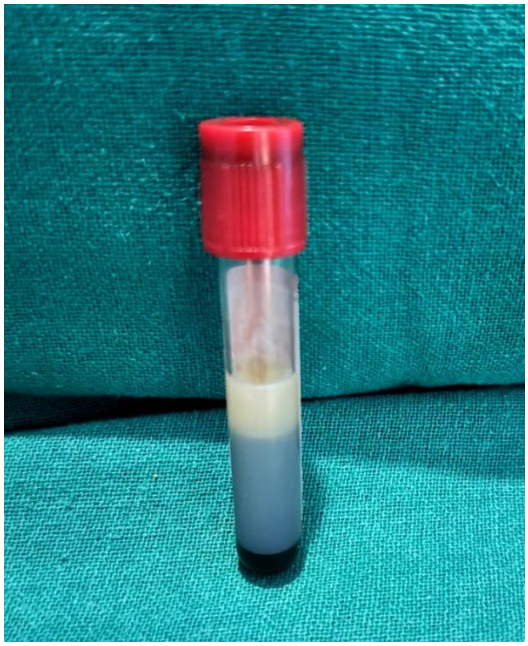

Figure 1: Groosly lipemic blood sample from the patient.

Given the circumstances, the patient was initiated on intensive outpatient management. A basal- bolus regimen of insulin was initiated along with oral antidiabetic medications to achieve rapid glycemic control. For dyslipidemia, fenofibrate 200 mg once daily and atorvastatin 20 mg once daily were prescribed. Dietary counselling was provided emphasizing a fat-restricted diet and appropriate lifestyle modification. The patient was closely monitored with regular clinical assessment and laboratory investigations.

During follow up, a marked and sustained reduction in triglyceride levels was observed. Over a period of 6 and 12 weeks, his TG level was reduced to 192 mg/dL and 164 mg/dL respectively. Glycemic control also improved significantly, with fasting blood glucose of 106 mg/dL and postprandial blood glucose of 170mg/dL. The patient did not report any symptoms during follow up period. Presently, is maintained on atorvastatin 20 mg once daily along with antidiabetic medication. Dietary advice and lifestyle modification measures are reemphasized.

This clinical observation underscores two important considerations. First, an uncontrolled Diabetes mellitus can a major contributor to extreme hypertriglyceridemia, and aggressive glycemic control plays a pivotal role in reduction of triglyceride levels. Second, although inpatient management remains the standard of care for severe hypertriglyceridemia, carefully supervised outpatient management may be pragmatic approach in selected cased where hospitalization is not feasible. Such approach requires close monitoring, strict adherence to dietary measures and pharmacotherapy, and clear communication regarding potential risks.

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We believe this case highlights real-world challenges faced in primary care, particularly in resource-limited settings. It emphasizes the importance of individualized, patient-centered decision-making while balancing guideline recommendation with practical constrains. Awareness of this potentially life-threatening condition and its appropriate management strategies is essential for all practicing physicians.

CONSENT TO PARTICIPATE

Written informed consent was obtained from the patient regarding publication of the data and images.

HUMAN ETHICS

All procedures performed in this study involving human participants were in accordance with the institutional review committee.

ETHICAL APPROVAL

Not Applicable.

CLINICAL TRIAL NUMBER

Not applicable

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

FUNDING

No source of funding to declare.

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