

# Plasmapheresis can correct refractoriness of insulin on triglyceride metabolism – A case report of hypertriglyceridemia-induced acute pancreatitis

Bala Sundaram <sup>1</sup>, Nabadwip Pathak <sup>2,\*</sup>, Sunil Kumar Nanda <sup>3</sup>

<sup>1</sup>Department of General Medicine, Pondicherry institute of medical sciences, Pondicherry, India. <sup>2</sup>Department of nephrology, Pondicherry institute of Medical sciences, Pondicherry, India. <sup>3</sup>Department of Biochemistry, Pondicherry institute of medical sciences, Pondicherry, India.

\*Correspondence: Nabadwip Pathak, Assistant professor, Department of nephrology, Pondicherry institute of Medical sciences, Kalathumettupathai, Ganapathichettikulam Village No.20, Kalapet, Puducherry 605014, India. Email: nabapthk88@gmail.com

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## ABSTRACT

Hypertriglyceridemia associated acute pancreatitis is a medical emergency and it causes significant morbidity and mortality. Here we report a case of 47 years old male with hypertriglyceridemia associated acute pancreatitis. The diagnosis was confirmed by elevated serum triglyceride levels and elevated lipase levels. Initially, Insulin infusion started with fibrates and statins but due to worsening hypertriglyceridemia and he underwent one session of plasmapheresis, following which triglyceride levels improved. Triglyceride assessment in removed plasma in plasmapheresis showed that the amount of triglyceride level reduction was 4 times the amount removed in plasmapheresis. The study showed that plasmapheresis improves insulin-related triglyceride metabolism besides removal.

**KEYWORDS:** Plasmapheresis; Insulin; Hypertriglyceridemia; Acute pancreatitis

## INTRODUCTION

Hypertriglyceridemia is the third leading cause of acute pancreatitis after gallstones and alcohol which causes significant morbidity and mortality. It accounts for 10% of all cases [1]. Treatment of hypertriglyceridemia involves lowering lipid levels by enhancing lipoprotein lipase activity through insulin infusions/plasmapheresis/heparin and/or fibrate therapy [2]. The removal of triglycerides via plasmapheresis was first described by Betteridge in 1978 [3]. Some studies with moderate-sample sizes reported approximately 80% reduction during the first plasmapheresis [4]. A recent randomized control study was done among 22 patients diagnosed as hypertriglyceridemia-induced acute pancreatitis in India, which compares the triglyceride reduction with insulin and plasmapheresis and this study shows no significant comparable differences except little greater trend in the decrease of triglycerides among plasmapheresis group [5]. To the best of our knowledge, there is no literature mentioning effect of plasmapheresis on the correction of refractoriness to insulin-related triglyceride metabolism in hypertriglyceridemia associated pancreatitis. We are reporting one case highlighting the effect of plasmapheresis on insulin-related triglyceride metabolism.

## CASE PRESENTATION

A 47-year-old male came to our emergency department with complaints of epigastric pain radiating posteriorly with associated vomiting for 2 days. He was hemodynamically stable at presentation. The blood investigations showed: a high level of triglyceride with 2205 mg/dl and a lipase level was 1090 with white blood cells 13,900/mm<sup>3</sup> and normal renal functions. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were normal. He was non-alcoholic, had no hypercalcemia, ANA was negative, and No imaging evidence of gall stones. Total cholesterol was 453 mg/dl, high-density lipoprotein (HDL) 10 mg/dl, Low-density lipoprotein (LDL) was 25, and serum triglyceride was 2205 mg/dl. HbA1c was 12.1%. USG abdomen and CT abdomen suggestive of acute pancreatitis with CT Severity score of 6/10. Based on the above information diagnosis of acute pancreatitis due to hypertriglyceridemia was made. The patient was started on a continuous infusion of ringer lactate 15ml/kg/hour, insulin infusion at the rate of 0.1 units/kg/hr, fenofibrate 360mg and atorvastatin 20mg once a day. Despite of 12 hours of medical management serum triglycerides increased to 3000mg/dl from 2205mg/dl, hence he underwent plasmapheresis. Body weight was 54 kg, and plasma volume calculation done as used by using formula used in study by Kaplan et al, it came as 3.5 liters [6]. Heparin-free plasma exchange done with 1 plasma volume removed without any complications over 1 hour [6]. Following plasmapheresis serum, triglyceride came down

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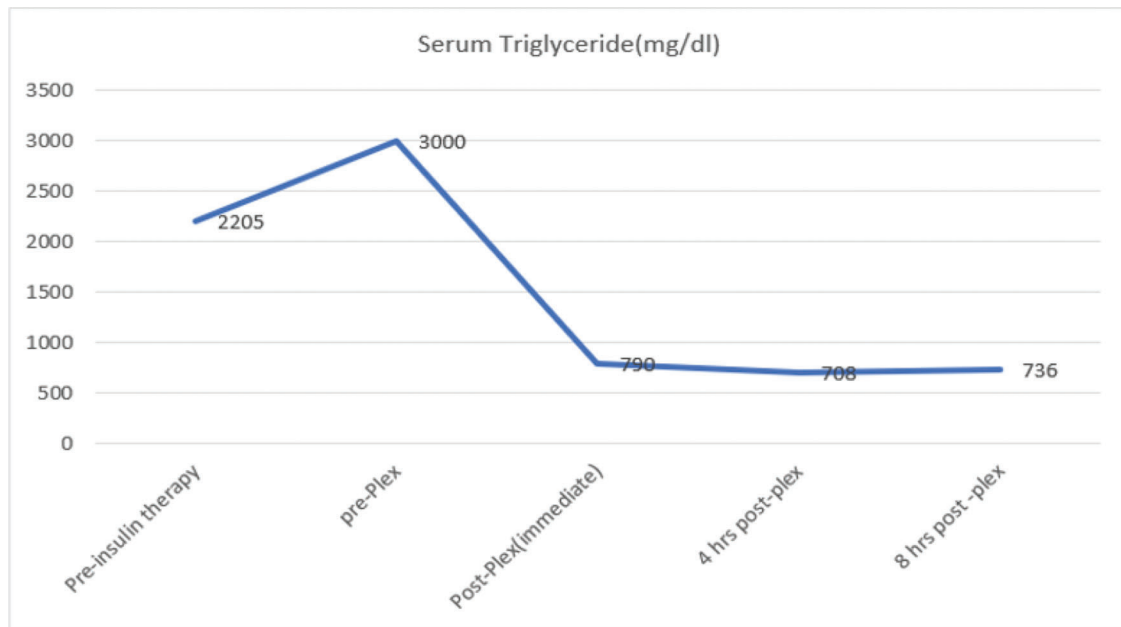


Fig. 1. Showing serum triglyceride trends during hospital course and its relation to mode of treatment.

to 790 mg% from 3000 mg% and subsequently further reduced (Figure 1). Removed plasma in plasmapheresis was sent for estimation of removed triglyceride which came as 21130 mg (Figure 2).

Subsequently no further plasmapheresis required and he responded to medical management.

## DISCUSSION

In hypertriglyceridemia-related pancreatitis, various drugs are being used: insulin infusion, fibrates, and statins [2]. The predominant enzyme which helps in the metabolism of triglyceride is lipoprotein lipase [2]. Insulin helps in hypertriglyceridemia treatment by stimulating lipoprotein lipase activity [7]. It takes at least 6 hours to increase lipoprotein lipase activity by acting as a modulator at mRNA level [8]. Hence, it is being used as a modality of treatment of hypertriglyceridemia-associated pancreatitis [9]. Lipoprotein lipase is active as a dimer and requires Apo-2 (present in VLDL and chylomicron) to be in an active state [9].

There is no significant difference in the rate of reduction of triglyceride levels between medical management using insulin therapy and plasmapheresis, but in cases refractory to medical management plasmapheresis is recommended. Therapeutic plasmapheresis has been used as a treatment modality with reasonable success [5,10] in hypertriglyceridemia associated acute pancreatitis. In our case, serum triglyceride increased from 2050 mg/dl to 3000mg/dl despite insulin infusion, statin, and fibrates for 12hrs, and pain abdomen also worsened. Due to the disease refractory to medical management as recommended by latest guidelines, he underwent 1 session of plasmapheresis [10].

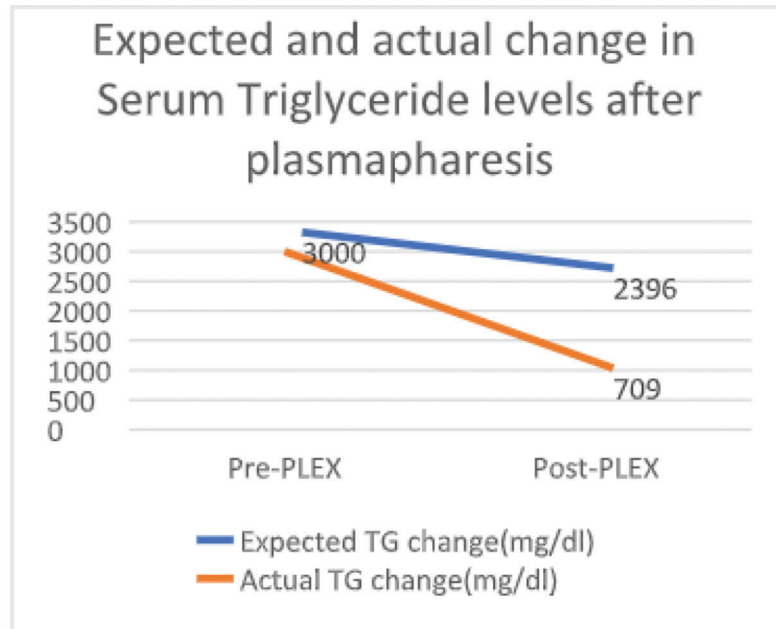
Total amount of triglyceride removed in plasmapheresis session was 21,130 mg (measured from plasma removed during plasmapheresis). Pre-plasmapheresis total triglyceride pool in the body was 105,000 mg (3000 mg/dl)

concentration in 3.5 liter-total plasma volume (equal to volume of distribution of triglyceride) [6]. Post plasmapheresis serum triglyceride was 709 mg/dl, (post plasmapheresis, total body triglyceride 24815 mg) which means total triglyceride reduction in body was 77,350 mg (Figures 1 and 2). The amount of triglyceride level reduction was almost 4 times the amount removed in plasma exchange. The possible reason for discrepancy between triglyceride removal and reduction could be because of improvement in responsiveness to medical management. As No dose modification was done in insulin dose and he was receiving medical management for more than 12 hrs. and as insulin takes 6hrs to show increase in lipoprotein lipase activity, it is less likely that insulin might have contributed to the above discrepancy [7]. Other drugs like statins, fibrates do not reduce triglyceride level so abruptly. There is a possibility that plasma exchange might have removed some reversible inhibitors of lipoprotein lipase or hepatic lipase improving insulin effect on triglyceride metabolism.

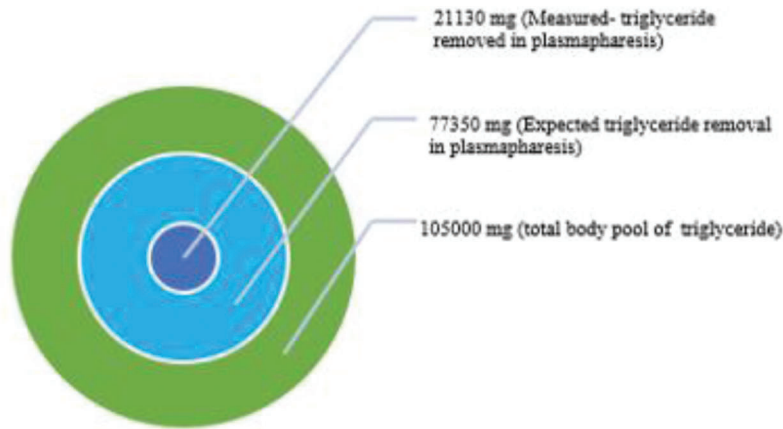
There are various factors which can influence the function of lipoprotein lipase in vivo like-Apo-C3, Apo-AV, Angiopoietin like protein (ANGPTL) 3 and 4 [11]. In vitro studies have shown that addition of any of the above cause inhibition of lipoprotein lipase [9]. N terminal end of AGNPLT 4 binds reversibly non competitively with lipoprotein lipase and converts it in to monomer from active dimer form [12].

Plasmapheresis can be beneficial for hypertriglyceridemia associated pancreatitis by reduction in cytokine levels beside beneficial due to removal of triglyceride [13].

To best of our knowledge, there is no study mentioning plasma exchange improving the responsiveness of insulin therapy in hypertriglyceridemia. As the literature of triglyceride kinetics during plasmapheresis is very less and to know exact factor whose removal might have contributed for the above phenomenon, we need further studies with a larger sample size.



A)



B)

**Fig. 2.** A. Showing changes in serum triglyceride (expected and actual) after plasma exchange. B. Venn diagram showing actual amount of triglyceride removed (measured from removed plasma) and expected amount of triglyceride removal (based on post plasmapheresis serum triglyceride). It explains the discrepancy between actual and expected post plasmapheresis serum triglyceride shown in A.

### CONCLUSION

Hypertriglyceridemia refractory to medical management can be treated by plasmapheresis. Plasmapheresis can improve the responsiveness of insulin therapy in the reduction of triglyceride levels in the management of hypertriglyceridemia-associated pancreatitis. More studies are needed to confirm the above statement.

### Conflict of Interests

The authors have no conflict of interests to declare.

### Acknowledgement

The authors of the present study sincerely thank all the medical staff who cooperated with us for completion of this study. All the data in this report was extracted from the patient’s hospital medical records.

### Ethical Statement

A written informed consent was obtained from the patient. All the authors declare that confidentiality of the patient was respected.

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There is no funding to the present study.

## Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author.

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