

# Severe hypertriglyceridaemia in pregnancy

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	Case 1 (TA)	Case 2 (PH)
Demographics	29yo G1P0 Indian ethnicity	27yo G2P1 Indian ethnicity
Past history	Nil	Acute pancreatitis 2° HTG in previous pregnancy, hypothyroidism, hepatitis C, gall stones
Family history	T2DM	Coronary artery disease in father (stents at age 53yo), recurrent pancreatitis in cousin
1 <sup>st</sup> presentation of pancreatitis	18/40, lipase 24,200 U/L (RI 20-210), TG 31.9 mmol/L (RI <1.7)	32/40, lipase 104 U/L (RI <60), TG 33.8 mmol/L
Presence of GDM	Diagnosed after 1 <sup>st</sup> presentation with pancreatitis	Diagnosed prior to 1 <sup>st</sup> presentation with pancreatitis
Treatment in pregnancy	Very low fat diet, fish oil, MCT Fasting, insulin/dextrose infusions	Very low fat diet, fish oil, MCT Fasting, insulin/dextrose infusions with attacks of pancreatitis Insulin aspart with meals for GDM
Progress	2 further admissions, given IV insulin/dextrose (1 <sup>st</sup> with pancreatitis, 2 <sup>nd</sup> pre-emptively for TG 31.8 mmol/L) TG range 6.7-39.1 mmol/L	1 recurrence of pancreatitis, treated with IV insulin/dextrose TG range 12.6-51.6 mmol/L
Delivery	SVD 35+5/40	ELUSCS at 36+6/40
Genetics	Compound heterozygous for lipoprotein lipase variants	Compound heterozygous for GPIHBP1 variants
Postpartum progress	Started on fenofibrate after cessation of breastfeeding Recurrence of pancreatitis Referred to lipid clinic for follow up	Referred to lipid clinic for follow up

# Severe hypertriglyceridaemia

- Defined as plasma TG > 11.4 mmol/L<sup>1</sup>
- Rare condition in pregnancy
- Known 2-4 fold increase in TG from baseline to third trimester<sup>2</sup>
- Primary: Genetic disorder (eg familial combined hyperlipidaemia and familial hypertriglyceridaemia, mutations in *LPL*, *apoC-II*, *LPL chaperone lipase mutation factor 1* and *GPIHBP1*, and familial dysbetalipoproteinaemia)<sup>3</sup>
- Secondary: Obesity, diabetes, alcohol, medications
- Complications include acute pancreatitis, hyperviscosity syndrome and preeclampsia with potential for maternal and fetal morbidity/mortality

1. Berglund L, *et al.* Evaluation and treatment of hypertriglyceridemia: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2012; 97: 2969-2989.

2. Goldberg AS, Hegele RA. Severe hypertriglyceridemia in pregnancy. *J Clin Endocrinol Metab* 2012; 97: 2589-2596.

3. Wong B, Ooi TC, Keely E. Severe gestational hypertriglyceridemia: A practical approach for clinicians. *Obstetric Medicine* 2015; 8: 158-167.

Treatment option	Mechanism	Benefit	Risk
Very low fat diet (<20% calories per day from fat)	Reduces substrate for exogenous TG synthesis	Effective	Difficult adherence, risk of maternal weight loss and fatty acid deficiency
Omega 3 3-4g daily	Reduce hepatic TG synthesis, increase fatty acid oxidation in the liver and skeletal muscle, enhance LPL activity	Reduce TG by 25-50%, helps avoid deficiency of key omega-3 fatty acids	GI side effects, lag time
MCT 10-30g daily	Not incorporated into chylomicrons	Source of calories, may benefit fetal brain myelination	Abdominal discomfort
Fasting and IV dextrose	Carbohydrate ingestion leads to a greater rise in plasma TG than IV	Aid in reversal of maternal weight loss	Inconvenient, effects short-lived
Insulin (generally IV)	Rapid and potent LPL activator	Immediate dramatic TG-lowering effect	Transient effect, unclear role for euglycaemic women
Fibrates Eg gemfibrozil 600mg BD	Transcription regulation by PPAR $\alpha$ , increase LPL mediated catabolism of VLDL, downregulate apoCIII expression	Effective gradual reduction of TG	Safety in pregnancy controversial, effect not immediate
Niacin 1500-3000mg daily	Inhibits fatty acid release and induces hepatic $\beta$ -oxidation of fatty acids	Deficiency during pregnancy is associated with congenital heart disease	Toxicity unknown at high doses (usual supplemental dose 18-30mg/day)
Heparin	Liberates LPL from endothelium	Limited data	Transient effects, ?depletion of LPL with chronic use
Plasmapheresis	Rapid removal of TG-rich lipoproteins and inflammatory mediators in pancreatitis	Immediate dramatic TG-lowering effect	Limited availability, high cost, risk of infection/thrombosis, transient effect

*Adapted from:* Wong B, Ooi TC, Keely E. Severe gestational hypertriglyceridemia: A practical approach for clinicians. *Obstetric Medicine* 2015; 8: 158-167 and Goldberg AS, Hegele RA. Severe hypertriglyceridemia in pregnancy. *J Clin Endocrinol Metab* 2012; 97: 2589-2596.

# Summary

- Severe hypertriglyceridaemia in pregnancy is a rare but important condition
- Various treatment modalities have been described
  - Very low fat diet and multidisciplinary team input recommended
  - Insufficient evidence to recommend one treatment over another
  - Fasting and intravenous dextrose/insulin were used in our patients due to lack of safety data with other therapies

# References

- Berglund L, Brunzell JD, Goldberg AC, Goldberg IJ, Sacks F, Murad MH, *et al.* Evaluation and treatment of hypertriglyceridemia: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2012; 97: 2969-2989.
- Goldberg AS, Hegele RA. Severe hypertriglyceridemia in pregnancy. *J Clin Endocrinol Metab* 2012; 97: 2589-2596.
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