Section: Miscellaneous

Original Research Article

EFFECT OF POSTPRANDIAL LIPEMIA ON NAFLD: A PILOT STUDY

Gautam Nath[1], Suvendu Kumar Mohapatra[2], Rakesh Kumar Barik[3]

[1]*Department of Gastroenterology, AHPGIC, Cuttack, Odisha, India.*
[2]*Department of Radio-Diagnosis, AHPGIC, Cuttack, Odisha, India.*
[3]*Department of Hepatology, S.C.B. Medical College, Cuttack, Odisha, India.*

Received *: 05/06/2025*
Received in revised form *: 26/07/2025*
Accepted *: 16/08/2025*

Corresponding Author:
Dr. Gautam Nath,
Assistant Professor, Department of Gastroenterology, AHPGIC, Cuttack, Odisha, India.
Email: gautamnath7@gmail.com

DOI: 10.70034/ijmedph.2025.3.466

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (3); 2538-2542

ABSTRACT

Background: NAFLD is a metabolic-related disorder characterized by fat infiltration of the liver in the absence of significant alcohol consumption. Clinically, NAFLD encompasses a broad spectrum of hepatic derangements ranging from fat accumulation (steatosis) to severe inflammation and fibrosis (NASH, non-alcoholic steatohepatitis) that can lead to cirrhosis.

Materials and Methods: We evaluated the postprandial lipemic response in 20 cases of NAFLD and compared it with 20 healthy age and gender matched controls. The subjects were given a standardised fat challenge following which, serial serum samples were estimated for TG level from zero to 8hour with 2hr interval, keeping baseline values of lipid.

Results: The Area under the curve (AUC) for triglyceride was calculated for the two groups using trapezoid rule, which showed a statistically significant ($p<0.001$) between the two groups (1814.20±166.46 vs 1341.25±153.36). As expected, the two groups showed a significant difference in baseline TG (177.15 ± 16.18 vs 128.3 ± 22.4), HDL (42.2 ± 6.13 vs 49.8 ± 4.39) and serum cholesterol (221.45 ± 31.26 vs 179.35 ± 26.59). The difference was found to be statistically significant ($p<0.001$).

Conclusion: This study not only demarcated the lipid infiltration in NAFLD cases but also showed the abnormal lipid metabolism on to a test meal suggesting a sluggish lipid clearance and prolonged serum lipemic response.

Keywords: NAFLD, NASH, Post Prandial Lipemia, Fatty Liver

INTRODUCTION

Metabolic disorders related to excess nutrient intake have been on the rise in recent decades. Increased incidences of metabolic syndrome, obesity and type II Diabetes Mellitus have lead to an increased awareness of the significance of co-morbidities associated with these non-communicable diseases, one of which is non-alcoholic fatty liver disease (NAFLD). NAFLD is a metabolic-related disorder characterized by fat infiltration of the liver in the absence of chronic alcohol consumption. Clinically, NAFLD encompasses a broad spectrum of hepatic derangements ranging from fat accumulation (steatosis) to severe inflammation and fibrosis (NASH, non-alcoholic steatohepatitis) that can lead to cirrhosis and subsequently to hepatocellular carcinoma. NAFLD is now more common than alcoholic liver disease owing to the rapid rise in the prevalence of obesity, and NAFLD is the most common cause of abnormal liver function tests.[1]

The concept of postprandial lipaemia was described way back in 1992 by Patsch et al to describe a positive correlation between CAD and plasma TG.[4] It was found that both the maximal TG increase and the magnitude of postprandial lipemia (area under the triglyceride curve (AUC) over 8 hours after the meal) were higher in cases than in control subjects. Since then, similar postprandial analyses have been carried out in T2DM (Ginsberg et al;2001),[5] Hypertension/Metabolic syndrome (Umpaichitra et al,[6] 2004) and NAFLD (Musso et al,[7] 2005, Lopez Miranda et al; 2007).[8]

The postprandial phase has been linked to atherosclerosis and increased oxidative stress in diabetes. Increased lipid peroxidation may have a role in the pathogenesis of NASH, alone or in association with insulin resistance and impaired adipokine signalling.[11] The liver takes up circulating

free fatty acid (FFA) in a dose-dependent fashion, and low-density lipoprotein (LDL) and remnants through the LDL-receptor and the liver-related receptor protein. Consistently, postprandial lipid storage contributes substantially to the liver triglyceride (TG) pool in NAFLD and the magnitude of postprandial lipaemia predicts liver steatosis.[10]
Although the mechanistic relationship between postprandial lipaemia and NAFLD is not clear, chylomicrons and their remnants, which are mainly present in circulation postprandially, can penetrate the endothelium and be retained in the sub-endothelial space,[2] where they may trigger the inflammatory reactions involved in pathogenesis of NAFLD.[3] Taken together, these findings suggest that exaggerated postprandial lipaemia may promote or proceed the development of NAFLD and metabolic syndrome.
In our study, we attempted the postprandial lipemic test in a selected group of NAFLD patients, proven through ultrasonography and clinical exclusion, along with healthy volunteers to compare.

MATERIALS AND METHODS

Twenty consecutive Patients with age range 30-60yrs attending our OPD during the years 2014-2016 with ultrasonographically proven hepatic steatosis and satisfying following criteria were selected:
Alcohol intake less than 20g/day, absence of autoimmune hepatitis (on the basis of clinical findings, raised globulin, AST/ALT ratio), absence of viral hepatitis (on the basis of serology for viral markers of HBV, HCV), absence of history of intake of any hepatotoxic drug like rifampicin, pyrazinamide, valproate, halothane, methyldopa, acarbose, protease inhibitors or any indigenous drug. The exclusion criteria used for both cases and controls for selection are target organ damage (cirrhosis, hepatocellular malignancy), deranged KFT (crCL<90), in-hospital major event requiring ventilator support, psychiatric illness, pregnant females, morbid obesity (BMI >35 kg/m2), chronic inflammatory conditions affecting the inflammatory response such as RA, SLE, tuberculosis, malignancy, patients on drugs affecting coagulation profile. Other Autoimmune disease, Wilson's disease and hemochromatosis was excluded based on detailed history and examination, subjects with fatal co-morbid conditions.
In the present study, we investigated the effect of a standardised fatty meal on plasma TG concentration in untreated cases of NAFLD and Healthy controls. To get the desired response, the standardization of the fat challenge was the most important aspect, after several cross references we adopted the diet standards mentioned by Patsch et al, which was applied on subjects with coronary artery disease4. Meal challenges rich in carbohydrates (>65%) have been shown to increase insulin levels but have shown no major effects in the postprandial lipid response9. The standardized fatty meal contained 729 kcal per square meter of body surface and consisted of 5.3 g protein, 24.75 g carbohydrate, 240 mg cholesterol, and 65.2 g fat (from heavy whipping cream).

Following recruitment into the study group subjects were admitted a day prior to fat challenge test in the hospital. Then after a complete clinical evaluation subjects were kept on overnight fasting. On the day of the study, each participant underwent a structured examination with special reference to demographic variables, dietary habits, physical activity and smoking status which included an interview, height, weight, WC and BMI were measured. A fasting IV access and an oral fat tolerance test (OFTT) was initiated.
Height and weight were measured to the nearest 0.5 cm and 0.1 kg, respectively. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. WC was determined to the nearest 0.1 cm using a measuring tape positioned at the midpoint between the lowest rib and the iliac crest and hips were measured at the largest gluteal circumference. These measurements were used to calculate WHR.
A catheter (20gz Helsingborg) was used to secure the IV access and the fasting blood samples were collected. Diluted heparin was used to maintain the patency of the IV catheter in order to perform serial sampling. Following fasting samples, subjects were provided with their respective standardized fat meals. They were instructed to consume the meal within a span of 10 to 15minutes, then to rest in their respective beds in the comfortable position and to refrain from strenuous physical activities, as the same may have an effect of post prandial lipemia. During the 8hrs of sampling subjects were only allowed to use the lavatory and intake of water if necessary. Postprandial blood samples were drawn at 2, 4, 6 and 8 hours from the IV access site.
Na-citrate containing 5-mL vacutainer tubes (for detection of fibrinogen) were placed on ice directly after blood sampling. Tubes were centrifuged at 3000rpm at 4˚ C for 15 min. Blood drawn in 5-mL vacutainer serum tubes (Becton Dickinson) was allowed to clot for 30 min at 218C. Subsequently, the serum tubes were centrifuged at 3000rpm for 15 min. Aliquots of plasma were frozen at −80°C for subsequent analysis of TG. Plasma total cholesterol and TG were measured by means of automated enzymatic methods.
The area under curve (AUC) for TG was computed using Trapezoid method (0-8hrs with 2hours of interval). Differences between groups for AUC were analyzed by repeated measures one way analysis of variance (ANOVA) followed by Bonferroni correction pairwise comparison for normally distributed variables.

RESULTS

A total of 178 OPD attending subjects were screened out of which 20 cases of NAFLD were recruited to study group and 20 healthy individuals were recruited to control group. The exclusion of individuals was based on excessive alcohol intake (40%), non-compliance for the consent for serial sampling (30%), history of hepatotoxic drug exposure (8%), history suggestive of autoimmune pathology (14%) and sero-positivity for HBV, Anti-HCV antibodies (8%) as confirmed by ELISA screening.

Out of 20 cases five were male subjects whereas rest are of female gender with an age range of 44.7 ± 6.38. The controls were matched for age, sex and BMI for better correlation of biochemical parameters with no statistical difference among the two. There was difference observed in systolic blood pressure with the case group (5mm of Hg) which was statistically insignificant (table:1).

Considering the fasting lipid profile, difference was observed between the groups in serum TG (177.15 ± 16.18 VS 128.3 ± 22.4), total cholesterol (221.45 ± 31.26 vs 179.35 ± 26.59) and HDL (42.2 ± 6.13 vs 49.8 ± 4.39). the difference found was statistically significant($p<0.001$). Summing up for the cases, a higher value was recorded for alkaline phosphatise which was statistically not significant (table:2). No difference was noted in the liver enzymes between the groups.

The postprandial lipemic response of the subjects were estimated using serum triglyceride (TG) level measurement considering the same being the most dynamic parameter considering fat challenge. The serial estimations were measured and plotted in the graph with horizontal axis being time and vertical axis being the TG level, for both study and control groups (fig:1).

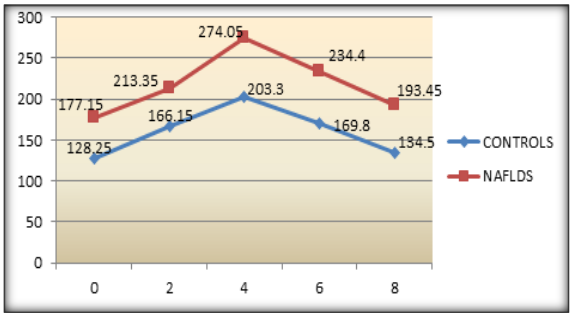

Figure 1: Line plots of postprandial triglyceride kinetics in NAFLD and control subjects

In relation to the administration of fat challenge and the peak lipemic response, it was observed that a peak level was achieved at 4-hour interval and the slope continued to decline further. It should, however, be realized that postprandial concentrations are the result of 2 main coinciding processes, e.g. absorption and clearance.

Considering the basal fasting levels for both the groups, a difference of 48.9mg% was observed between both groups suggesting an existence of dyslipidaemia in the study groups further adding to the reason of impaired lipid metabolism. The serial estimations of TG at 2 hourly intervals have also shown a significant difference in serum TG levels between cases and control groups with ($p<0.001$).

To calculate the magnitude of lipaemia, the Area under the curve (AUC) was calculated for the two groups using trapezoid rule, which showed a statistically significant ($p<0.001$) between the two groups (1814.20±166.46 vs 1341.25±153.36).

Comparison was attempted by reclassifying the study groups on the basis of gender, presence of diabetes mellitus and metabolic syndrome, but the difference was not found to be statistically significant($p>0.005$).

Table 1: Anthropometric variables

VARIABLE		CONTROL (n = 20)	CASES (NAFLD) (n = 20)	p- VALUE*
Age		42.75 ± 7.28	44.7 ± 6.38	0.374
Sex	Male	5	5	1.0
	Female	15	15	
Waist.Cirm (c.m)		88.4 ± 7.25	93.95 ± 10.56	0.06
W.H.R		0.90 ± 0.06	0.92 ± 0.06	0.445
BMI (kg/m^2)		23.4 ± 2.36	24.79 ± 2.25	0.063
SBP		122.6±4.26	127.6±45.5	0.32
DBP		86±2	77.4±27.42	0.063

Table 2: Biochemical variables of cases and controls

PARAMETERS	NAFLDS(n=20)	CONTROLS(n=20)	P value
S. CHOLESTEROL(mg/dl)	221.45 ± 31.26	179.35 ± 26.59	<0.001
S.HDL (mg/dl)	42.2 ± 6.13	49.8 ± 4.39	<0.001
S. TRIGLYCERIDE(mg/dl)	177.15 ± 16.18	128.3 ± 22.4	<0.001
S. AST	24.35 ± 3.25	22.65 ± 5.65	0.554
S. ALT	30.54 ± 4.27	34.96 ± 3.12	0.367
S. ALP	274.35 ± 25.32	215.65 ± 21.56	0.495
TG 2(mg/dl)	213.35 ± 22.76	166.2 ± 20.91	<0.001
TG4(mg/dl)	274.05 ± 25.65	203.3 ± 17.61	<0.001
TG6(mg/dl)	234.4 ± 21.99	169.8 ± 19.91	<0.001
TG8(mg/dl)	193.45 ± 19.52	134.5 ± 20.31	<0.001

DISCUSSION

NAFLD is a pathology that involves several metabolic abnormalities, such as hyperinsulinemia, IR, increased cytokine secretion and abnormalities in the postprandial state.[7] Delayed fat clearance was also observed in patients with diabetes mellitus (DM), particularly in the presence of obesity/MetS.[6] Delayed postprandial lipid clearance has been observed in adults with NAFLD,[7] how this might contribute to disease pathology is not completely understood.

Obesity is associated with a range of metabolic abnormalities including fasting and postprandial dyslipidaemia. Visceral adiposity with increased intraabdominal fat has been shown to precede the development of insulin resistance. The IR is associated with dyslipidaemia and may affect chylomicron remnant metabolism by down regulating LDL-receptor expression and increasing hepatic cholesterol synthesis and very low-density lipoprotein secretion. These effects increase competition between chylomicron and very low density lipoprotein remnants for hepatic receptors, thereby impairing the uptake of chylomicron remnants by this pathway.[12] These changes result in elevated postprandial TG levels. NAFLD, steato-hepatitis and IR have similar potential effects on chylomicron remnant metabolism.

We found that subjects with NAFLD have an altered response to a fatty meal when compared to Healthy controls. The fasting TG values were 38% higher in NAFLD compared to Healthy subjects ($p<0.001$). The observed difference was smaller than that reported by Chan et al; 2003.[13] Several facts could explain this difference: First, the fasting TG levels in their control group were much lower compared to our group. Fasting TG levels of their MetS subjects were also lower even though the BMI was higher.

Area under the curve to define the magnitude of lipaemic response for both the groups was significantly higher in NAFLD when compared to controls (1814.20±166.46 vs 1341.25±153.36). The difference was statistically significant ($p<0.001$), suggesting a delayed TG clearance from the peripheral blood following fat challenge. In most instances after 8 hours of OFTT the TG returned to the baseline value, where as in NAFLD subjects there was a higher value noted even after 8hours (10%). Similar results were shown in a study conducted by Musso g et al; 2003, but the amplitude of lipaemia was on the lower side considering our study. The difference could be explained by the fact that the fat challenge used for the said study was devoid of any carbohydrate component which is very essential for effective absorption of the dietary fat8. Further a low baseline TG was recorded in that study for NAFLD subjects (100 ± 44 vs 177.15 ± 16.18), which might have led to a decreased lipaemia response. Postprandial lipid responses were similar between NAFLD and obese control subjects, but differed from lean subjects. Lean subjects cleared TG from plasma within 8 hours, but both obese and NAFLD subjects had a delayed clearance.

Furthermore, the regulation of plasma TG in NAFLD subjects may differ according to concomitant characteristics. Findings from the current study also demonstrated an enhanced TG rise postprandially not only in patients with DM (Ginsberg et al; 2001), but also in patients with obesity and increased BMI, the difference in basal fasting level of TG found in cases of NAFLD with DM (15.37mg%) and in cases of NAFLD with BMI>23(20.01mg%) and BMI>25(22.2mg%), in Comparison with lean NAFLD subjects, signifying the additive metabolic deranging effects of DM/obesity in the pathophysiology of NAFLD. The existence of metabolic syndrome in the case group should never be overlooked.

As we screened the subjects for recruitment, we also evaluated them for parameters like WC, FBS, TG, HDL and BP in order to determine the prevalence of MetS in this group of people. Not surprisingly, a prevalence of 70% was noted with additional 15% of cases satisfying two out of five criteria for MetS (AHA guidelines), signifying the co-existence of this condition with NAFLD. In order to determine the existence of abnormal OFTT response if any, we compared the PPL response of patients with MetS and NAFLD against those who had NAFLD only. Though the results were statistically not significant ($P=0.435$), a higher baseline TG was recorded in MetS subgroup (112%) along with a more exaggerated lipemic response with a higher AUC (1865.56 vs 1787.25).

It is possible that our NAFLD population due to the hyper insulinemic state exhibits an imbalance between influx and efflux to and from the liver; therefore, the high availability of TG in the liver could promote an increased VLDL Apo B-100 secretion. Additionally, the meal challenge composition may be influencing the postprandial response. Studies suggest that meals rich in SFA evoke higher TG concentrations due to a possible altered secretion and degradation when compared to meals rich in poly unsaturated fatty acid (PUFA) and mono unsaturated fatty acid (MUFA).[14] Meals higher in SFA will delay CM remnants clearance, promote fatty acid availability in the liver and consequently impair Apo B-100 secretion and therefore VLDL hepatic secretion (Musso et al., 2003). It is possible that subjects with NAFLD may be more susceptible to the adverse postprandial affects observed after a high SFA meal.

From the serial TG estimations of the study groups, we did observe that the maximum rise in serum TG value was noted at four hour mark of the sampling serial, which is in accordance with the process of assimilation. Further, except for one subject in the control group with a serum TG value of 251mg% at 4hr, none has been recorded with a serum TG of greater than 240mg%. While on the other group, all the subjects showed a serum TG value of greater than

240mg% at 4hr following OFTT. Whether this value could be measured as a reference value, was not been validated as because of the small sample size (n=20) of the study group.

Postprandial triglycerides have been found to be an independent risk factor of cardiovascular disease in larger population studies and were most useful when levels were determined around 4hr postprandial.[15] Larger-scale studies may determine whether a routine blood triglycerides test at 4 h after a standardised fat meal may help identify individuals at risk of developing NAFLD and hence the metabolic syndrome. Which could possibly make postprandial TG a surrogate marker of NAFLD, like the postprandial blood glucose for diabetes mellitus.

CONCLUSION

Postprandial metabolic response may be mostly affected by chronic intake and general lifestyle; rather than acute changes in food intake, this chronic event leads to decreased efficiency of handling serum lipids. This delayed lipid clearance in addition to the hyperlipaemic state present in cases with NAFLD may have promoted a pro-inflammatory environment which would worsen the hyperinsulinemic state leading to a vicious cycle characterized by delayed lipid clearance and a pro-inflammatory environment. Further studies are needed to get a better outlook of this pathological entity.

REFERENCES

1. Sattar N, Forrest E, Preiss D. Non-alcoholic fatty liver disease. BMJ. 2014 Jul 29;349:g4596.
2. Proctor SD, Mamo JC. Retention of fluorescent-labelled chylomicron remnants within the intima of the arterial wall--evidence that plaque cholesterol may be derived from post-prandial lipoproteins. Eur.J Clin.Invest 1998;28:497–503.
3. Targher, G., Pichiri, I., Zoppini, G., Trombetta, M., & Bonora, E.Increased prevalence of cardiovascular disease in Type 1 diabetic patients with non-alcoholic fatty liver disease. J Endocrinol Invest 2012, 35(5), 535-540.
4. Patsch JR, Karlin JB, Scott LW, Smith LC, Gotto AM Jr: Inverse relationship between blood levels of high density lipoprotein2 and magnitude of postprandial lipaemia. Proc Natl Acad Sci USA 1983;80:1449-1453.
5. Ginsberg HN, Illingworth DR: Postprandial dyslipidemia: anatherogenic disorder common in patients with diabetes mellitus. Am J Cardiol 2001, 88:9H-15H.
6. Umpaichitra V, Banerji MA, Castells S. Postprandial hyperlipidemia after a fat loading test in minority adolescents with type 2 diabetes mellitus and obesity. J Pediatr Endocrinol Metab. 2004; 17: 853-864.
7. Musso G, Gambino R, De Michieli F, Cassader M, et al. Dietary habits and their relations to insulin resistance and postprandial lipaemia in nonalcoholic steatohepatitis. Hepatology. 2003; 37 (4): 909-916.
8. Lopez-Miranda J, Williams C, Lairon D. Dietary, physiological, genetic and pathological influences on postprandial lipid metabolism. Br J Nutr. 2007 Sep;98(3):458-73.
9. 68. Kapur S, Groves MN, Zava DT, Kapur S. Postprandial Insulin and Triglycerides after Different Breakfast Meal Challenges: Use of Finger Stick Capillary Dried Blood Spots to Study Postprandial Dysmetabolism. Diabetes Sci Technol. 2010; 4 (2): 236-243.
10. Musso G, Gambino R, Durazzo M, Biroli G, Carello M, Faga` E, et al. Adipokines in NASH: postprandial lipid metabolism as a link between adiponectin and liver disease. HEPATOLOGY 2005;42:1175-1183.
11. Farrell GC, Larter CZ. Nonalcoholic fatty liver disease: from steatosis to cirrhosis. HEPATOLOGY 2006;43:S99-S112.
12. Kolovou, G., Anagnostopoulou, K., & Cokkinos, D. Pathophysiology of dyslipidaemia in the metabolic syndrome. Postgraduate Medical Journal 2005 81(956), 358–366.
13. Chan DC, Watts GF, Barrett PH, O'Neill FH, Redgrave TG, Thompson GR: Relationships between cholesterol homoeostasis and triacylglycerol-rich lipoprotein remnant metabolism in the metabolic syndrome. Clin Sci (Lond) 2003, 104:383-388.
14. Jackson KG, Wolstencroft EJ, Bateman PA, Yaqoob P, et al. Acute effects of meal fatty acids on postprandial NEFA, glucose and apo E response: implications for insulin sensitivity and lipoprotein regulation?. Br J Nutr. 2005; 93 (5): 693-700.
15. Bansal S, Buring JE, Rifai N, Mora S, Sacks FM, Ridker PM. Fasting compared with nonfasting triglycerides and risk of cardiovascular events in women. JAMA. 2007;298(3):309–16.