ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 8 | August - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

POSTPRANDIAL LIPEMIA: DELAYED CLEARANCE OF LIPIDS IN METABOLIC SYNDROME.

Biochemistry

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ABSTRACT

Introduction:- Metabolic syndrome , as well as postprandial hypertriglyceridemia, is associated with coronary heart disease. The number of meals consumed and the long duration of postprandial lipemia lead to a continual fluctuation in the degree of lipemia throughout the day. **Objective:-** The present study aimed to assessed the postprandial lipemia after OFTT in MetS and control. Fasting and postprandial lipid profile was measured in (n=31) MetS and (n=18) control. MetS group were subdivided according to fasting TG concentration either <or ≥ 1.7 mmol/L. **Results:-** Postprandial lipemia was assessed by an OFTT and area under the curve (AUC). MetS had significantly higher ($p<0.0001$) fasting lipid profiles, postprandial responses ($p<0.001$) during OFTT and AUCs ($p<0.001$) than control. The level peaked at 6 hours after fat load ($p<0.001$). MetS with fasting TG ≥ 1.7 mmol/L had greater postprandial responses ($p<0.001$) and higher AUC ($p<0.0001$) than patients with TG <1.7 mmol/L. The most significant correlation was between AUCs TG with fasting TG and VLDL of MetS. **Conclusion:-** We concluded that fasting TG concentration is the main determinant of postprandial lipemia, we found significant postprandial hypertriglyceridemia and delay in postprandial triglyceride clearance in MetS.

KEYWORDS

Metabolic syndrome, Cardiovascular Disease, Insulin resistance, Oral fat tolerance test, Postprandial lipemia

INTRODUCTION:-

Metabolic syndrome is a disorder of energy utilization and storage. The metabolic syndrome is a cluster of several vascular risk factors (impaired glucose metabolism, dyslipidaemia, hypertension and central adiposity). Reaven et al.[1] proposed insulin resistance as the underlying metabolic aberration linking essential hypertension (HTN), dyslipidemia, type 2 diabetes and other abnormalities associated with an increased risk of atherosclerotic cardiovascular disease in adults. This constellation is now designated as the metabolic syndrome (Mets). Since then, many epidemiological studies have shown that MetS is associated with an increased incidence of coronary heart disease (CHD) [2,3]. Atherosclerosis is the primary cause of death in the world. The hypothesis proposed by Fraser [4] that atherosclerosis is a postprandial phenomenon that largely depends on the metabolic response to the ingestion of food. The number of meals consumed and the long duration of postprandial lipemia lead to a continual fluctuation in the degree of lipemia throughout the day. Postprandial hyperlipidemia with accumulation of remnant lipoproteins is common metabolic disturbances associated with atherosclerosis and vascular dysfunction, particularly during chronic disease states such as obesity, diabetes and MetS [5].

The associations between metabolic abnormalities and cardiovascular disease have been studied largely during fasting conditions. However, the important contribution of postprandial state to cardiovascular disease is increasingly being recognized, particularly in conditions of insulin resistance and T2DM. In fact, in contemporary post-industrialized societies most individuals spend the majority of non-sleeping hours in the postprandial state. As the typical American diet consists of 3 or more meals per day and it takes more than 8 hours for triglyceride concentrations to return to fasting levels after a meal, postprandial triglyceride concentrations often remain elevated throughout the day. Importantly postprandial triglyceride concentrations may in fact be a better predictor of cardiovascular events than fasting triglycerides. The adverse effect of postprandial triglycerides is thought to be mediated by proatherogenic lipolysis products of nascent triglyceride-rich lipoproteins, such as remnant lipoproteins and fatty acids, and even a transient increase in these factors may worsen vascular function [6]. Following a fat enriched meal, chylomicrons rapidly increase and lead to pronounced triglyceride elevations peaking approximately 3-6 hours post-meal [7].

Insulin resistance and compensatory hyperinsulinemia lead to overproduction of very low density lipoprotein particles. A relative deficiency of lipoprotein lipase, an insulin sensitive enzyme is partly responsible for the decreased clearance of fasting and postprandial TRLs, and the decreased production of HDL particles. The competition for enzyme is most likely when fasting hypertriglyceridemia is present. The increased levels of free fatty acids (FFAs) as a result of hypercaloric diet are regarded as one of the key etiologic components of the metabolic syndrome, type 2 diabetes mellitus and obesity [8]. The resulting increased concentration of cholesteryl ester rich fasting and postprandial TRLs is the central lipoprotein abnormality of the metabolic syndrome.

Postprandial hyperlipidemia has many negative effects on vascular integrity, inflammation, and fatty acid metabolism but can be positively influenced by dietary patterns, food composition, conditions associated with lifestyle (physical activity, smoking and alcohol consumption), physiological factors (age, gender, and gender background). Since postprandial lipemia is a physiological response to a fatty meal, it could be predicted that it would be influenced by the amount and type of fat in the diet, and there is strong evidence to support this [9].

Postprandial hyperlipidemia may be a link between lifestyle choices and the current alarming rise in the incidence of obesity, insulin resistance, T2DM, and CVD [10]. A Meta-analysis involving 87 studies, which included 951,083 patients based on the definitions of metabolic syndrome by the 2001 National Cholesterol Education Program (NCEP) and 2004 revised National Cholesterol Education Program (rNCEP) demonstrated a 2-fold increase in cardiovascular outcomes and a 1.5-fold increase in all-cause mortality in subjects with the metabolic syndrome [11].

In the same context little is known, however, about the occurrence of postprandial lipemia in Metabolic syndrome cases. The main aim of this study was to assess the postprandial response to an oral fat load test in Metabolic syndrome patients.

MATERIAL AND METHODS:-

The study was carried out at the Department of Biochemistry M.G.M. Medical College, Indore. Collaboration of the Department of Medicine at MY Hospital was sought in the provision of cases. Volunteer patients diagnosed with the Metabolic syndrome in the clinics of the department were selected for the study. Complete care was taken in protecting the anonymity of patients and the privacy of patient medical records. The study did not involve administration of any drug/medication or any surgical procedure to the patients. Forty patients (29 men and 11 women) with documented Metabolic syndrome, of whom 31 patients (23 men and 8 women) , and Eighteen control subjects (12 men and 6 women) agreed to take part. All of the patients had significant Metabolic syndrome, none of the control

subjects had evidence of coronary atherosclerosis on coronary angiography. The majority of patients (77.4%) hypertensive and (87%) were diabetic; and they were taking antihypertensive and cholesterol lowring and glycemic control medication at the time of the study. Patients who had HIV-positive status, liver disease, renal disorder, thyroid disorder, hormonal disorder and and smoking more than 20 cigarettes per day excluded from the study.

Definition of the metabolic syndrome:-

To identify cases of metabolic syndrome the ATP III (Adult Treatment Panel III) criteria [12] were used i.e. the presence of three or more of the following five characteristics:

1. Elevated triglycerides (>150 mg/dl) or specific treatment for this lipid abnormality.
2. Reduced HDL cholesterol (<40 mg/dl in males and <50 mg/dl in females) or specific treatment for this lipid abnormality.
3. High blood pressure (>130/85 mm/Hg) or on treatment for hypertension.
4. Raised fasting blood glucose (>100mg/dl or 5.6 mmol) or already having type II diabetes.
5. Obesity- measured as waist circumference >35 inches in women and >40 inches in men or BMI 25-30 Kg/m2 (obesity or overweight).

Design of study:-

The night before the test, participants were asked to refrain from smoking and to fast for 12 hours. On the day of the study, each participant underwent a structured examination, which included an interview. Height, weight, WC and , a fasting venipuncture and an oral fat tolerance test (OFTT) were done. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. Questionnaires were used to obtain information on demographic variables, medical history, medication use, dietary habits, physical activity and smoking status. A consent was taken by each subjects prior to entering into the study. A detailed history and physical examination was carried out for every subjects who entered into the study as per designed proforma.

Blood samples collection:-

Only blood samples collected in the Clinical Biochemistry laboratory were used for in vitro biochemical analysis. The samples were collected by standard procedures under aseptic conditions. Standard procedures were followed for the preservation and storage of samples before analysis.

Oral fat tolerance test (OFTT):-

All patients attended the hospital at 7.00-8.00 AM after a overnight fast, than an intravenous catheter was inserted into a forearm vein for blood sampling. The OFTT was performed as described by Patsch et al.[13] with a slight modification of the fatty meal. Briefly, it consisted of cream, chocolate-flavoured syrup, sugar and powdered milk, which provided energy from fat (83.5%), carbohydrates (14%) and protein (2.5%). The meal was consumed within 20 min, after which the participants were instructed not to take anything orally, except water, for the subsequent eight hours. Administration of any oral drugs and intravenous infusion was prohibited until the last blood sample was collected. Lipid profiles comprising TC, HDL cholesterol, and TG concentrations were measured at baseline (defined as the value at 0 h) and at 2 h, 4 h, 6 h and 8 h post-load.

Laboratory measurements:-

Serum concentrations of Total Cholesterol by CHOD/PAP method [14], High density lipoprotein cholesterol by Direct enzymatic method [15], Triglycerides by GPO/PAP method [16] and plasma glucose were measured by GOD-POD enzymatic colorimetric method [17] using a semi-automated clinical analyser. Calculation of Low density lipoprotein cholesterol and very low density lipoprotein concentrations were based on the Friedewald equation. Serum insulin level was measured by the ELISA [18] and degree of insulin resistance was calculated by the Homeostasis model assessment (HOMA) index which was computed by the formula: FBS (mmol/L)* serum insulin (µU/ml)/22.5.

Statistical analysis:-

Data analysis was done using the IBM SPSS Statistics version 20 and MedCalc version 14 program with a value of $p<0.0001$, $p<0.01$ and $p<0.05$ considered highly significant and significant respectively. Two groups comparison was done by the student's paired or unpaired t-test and the test for parametric or non parametric data. Results are expressed as Mean ± SD. For repeated measures within a group , One-way analysis of variance (ANOVA) was used to assess any differences between the means of variables. Area under the curve (AUC) for serial measurements of triglyceride concentrations at baseline (0 hour) and after the fat load (2h, 4h, 6h and 8 hours) was calculated using the trapezoid rule [19]. Linear regression analysis and correlation coefficient analysis were performed to reveal any significant relation between the determinants of post prandial lipemia.

RESULTS:-

Metabolic syndrome patients (n = 31) and control subjects (n = 18) were matched for age , BMI , WC and Blood pressure, all $P < 0.05$. Measurements of risk factors for MetS were assessed according to the ATP III criteria. The group with MetS was further divided into patients who had a fasting TG concentration either ⩾1.7 mmol/l (MetS +veTG, n = 15) or <1.7 mmol/l (MetS −veTG, n = 16).

Table 1 represents the anthropometric data, fasting biochemical variables and clinical characteristics of the groups of patients with MetS and the control subjects. Mean BMI, WC, BP systolic and diastolic were significantly higher in MetS compared than the control subjects ($P < 0.001$).

Fasting lipid profiles showed that patients with MetS had significantly ($p<0.0001$) elevated mean LDL-C , VLDL and TG, and Glucose, Insulin, Insulin resistance levels than the control subjects, and total cholesterol was slightly increased while HDL-C concentrations was lower in MetS than control subjects, but not significantly so. Most of the patients with MetS (77.4%) had hypertension and were taking antihypertensive medication, and (87%) had diabetes. Nine metabolic patients (29%) smoked less than 20 cigarettes per day.

Table 1: Anthropometric data, fasting biochemical variables and clinical characteristics of the main study groups

Variables	Unit	MetS (n=31)	Control (n=18)
Age	Years	50.64 ± 10.70	36.51 ± 6.65
WC	Cms	95.24 ±7.13*	83.21 ± 4.64
BMI	Kg/m2	26.15 ± 5.48*	21.11 ± 3.30
BPS	MMHg	136.04 ± 12.1*	117.41 ± 2.91
BPD	MMHg	92.12 ± 6.91*	81.23 ± 1.32
Glucose	mmol/L	8.96 ± 1.60*	04.89 ± 0.46
Triglycerides	mmol/L	2.10 ± 1.17*	1.34 ± 0.96
Total Cholesterol	mmol/L	4.71 ± 2.70	3.76 ± 0.54
HDL-C	mmol/L	1.15 ± 0.29	1.22 ± 0.24
LDL-C	mmol/L	3.13 ± 0.84*	2.27 ± 0.55
VLDL	mmol/L	0.42 ± 0.54*	0.26 ± 0.10
Insulin	µU/ml	12.84 ± 1.26*	7.93 ± 0.81
HOMA IR		5.62 ± 1.31*	1.90 ± 0.29
Hypertension		77.4% (24)	--
Diabetic		87% (27)	--
Cigarette smoking		29% (9)	--

Data are expressed as mean ± SD or %.

MetS: metabolic syndrome; WC: waist circumference; HDL: high density lipoprotein cholesterol; LDL: low density lipoprotein cholesterol; VLDL: very low density lipoprotein cholesterol, HOMA IR: homeostatic model assessment Insulin resistance.

Table 2 Lipid profiles of the main study groups measured at baseline and during the oral fat tolerance test

Variables	MetS (n=31)	Control (n=18)	f-ratio
TC	4.71 ± 1.13	3.76 ± 0.54	5.971*
0h	4.78 ± 1.10	3.89 ± 0.56	
2h	4.86 ± 1.10	3.98 ± 0.48	
4h	4.97 ± 1.09	3.97 ± 0.56	
6h	4.83 ± 1.03	4.14 ± 0.58	
8h			
HDL-C	1.15 ± 0.29	1.22 ± 0.24	1.605
0h	1.12 ± 0.29	1.09 ± 0.28	
2h	1.10 ± 0.31	0.96 ± 0.18	
4h	1.06 ± 0.28	0.95 ± 0.29	
6h	1.07 ± 0.27	1.08 ± 0.22	
8h			
LDL-C	3.13 ± 0.98	2.27 ± 0.50	5.252*
	3.08 ± 0.95	2.31 ± 0.49	

0h	3.04 ± 0.93	2.40 ± 0.39	11.315*
2h	2.99 ± 0.90	2.29 ± 0.43	
4h	3.11 ± 0.87	2.56 ± 0.50	
6h			
8h	2.10 ± 1.18	1.34 ± 0.96	
Triglycerides	2.83 ± 1.13	2.40 ± 1.40	
0h	3.57 ± 1.14	3.04 ± 1.66	11.315*
2h	4.54 ± 1.15	3.63 ± 1.90	
4h	3.22 ± 1.16	2.46 ± 1.78	
6h			
8h	0.42 ± 0.23	0.26 ± 0.19	
VLDL	0.56 ± 0.22	0.48 ± 0.28	
0h	0.71 ± 0.22	0.61 ± 0.33	
2h	0.90 ± 0.23	0.72 ± 0.38	
4h	0.64 ± 0.23	0.49 ± 0.35	
6h			
8h			

Data are expressed as mean ± SD. Results are presented in mmol/l.

P values were determined by repeated measures ANOVA and denote difference within each group. (* p<0.001)

MetS: metabolic syndrome; TC: total cholesterol; HDL: high density lipoprotein cholesterol; LDL: low density lipoprotein cholesterol; VLDL: very low density lipoprotein 0 h: baseline concentration; 2 h, 4 h, 6 h, 8 h: concentrations at 2, 4, 6 and 8 hours after the fat load.

Oral fat tolerance test (Postprandial lipid profile Table 2):-

Oral fat tolerance test was performed followed by giving standard fatty meal to obtain the AUCs for triglycerides and collected blood samples from baseline to specific time interval.

Patients with metabolic syndrome (n=31) and control (n=18) measured at baseline and various time interval during the OFTT were shown in Table 2. The postprandial lipid profile was taken every 2h interval after fasting determination. Table 2 showed that TG level during the OFTT was significantly increased in 2h, 4h, and 6h from the baseline in both group and peak level of TG was found at the 6h and this was significantly (p<0.001) (figure 1.1) increased in Metabolic syndrome cases compared to control group. And at 8h the level decreases.

Same changes was observed in case of total cholesterol, VLDL (figure 1.2), LDL-C level, it showed the significant changes between the time interval and the peak level was found at 6h this was significantly (p<0.001) increased in metabolic syndrome cases compared to control subjects . In contrast, the levels of HDL-C was showed the postprandial changes during various time interval in OFTT, but there was no significant changes observed between time interval from the baseline. These showed the unspecific variation from the 0h to 8h samples.

Postprandial responses in patients with MetS and baseline TG ⩾ or <1.7 mmol/l:-

Postprandial responses during the OFTT in patients with MetS and baseline TG concentration either ⩾1.7 mmol/l (MetS +veTG) or <1.7 mmol/l (MetS −veTG), and control subjects are shown in Table 3. Significant differences were found between the three groups before and after the fat load (ANOVA all P < 0.0001). Mean TG concentrations were significantly increased in the MetS +veTG patients compared with the MetS −veTG patients, and also in the MetS +veTG patients compared with the control subjects at all time points (0 h P < 0.0001; 2 h, 4 h, 6 h and 8 h P < 0.001). No significant differences were found between MetS −veTG patients and control subjects at any time point (P > 0.05).

Table 3: Oral fat tolerance test showed postprandial lipid profile for Metabolic syndrome having baseline triglyceride concentration either ⩾1.7 mmol/l (MetS + veTG) or <1.7 mmol/l (MetS −veTG) and control subjects

	MetS+ve TG TG≥150mg/dl n=15	MetS-veTG TG≤150mg/dl n=16	Control n=18
Triglycerides (mmol/L)	3.08 ± 0.96**	1.19 ± 0.29	1.34 ± 0.96
0h	3.67 ± 0.85*	2.04 ± 0.71	2.40 ± 1.40
2h	4.46 ± 0.85*	2.73 ± 0.60	3.05 ± 1.66
4h	5.42 ± 0.94*	3.70 ± 0.57	3.63 ± 1.90
6h	4.18 ± 0.74*	2.32 ± 0.63	2.46 ± 1.78
8h			

Data are expressed as mean ± SD.

**P < 0.0001 for MetS +veTG patients vs. MetS −veTG patients and control subjects at 0 h; *P < 0.001 for MetS +veTG patients vs. MetS −veTG patients and control subjects at 2 h, 4 h, 6 h and 8 h.

MetS: metabolic syndrome; TG: triglycerides;

0 h: baseline concentration; 2 h, 4 h, 6 h, 8 h: concentrations at 2, 4, 6 and 8 hours after the fat load.

Area under the curve:-

Mean AUCs for TG and VLDL in MetS patients group were significantly higher than in the control subjects (mean ± SD of patients with metabolic syndrome vs. Control subjects in mmol*h/l = 27.2 ± 9.51 vs. 21.96 ± 7.12 , P<0.001, respectively for TG (figure 2) and 5.40 ± 2.81vs. 4.37 ± 2.06, p<0.001, respectively for VLDL). AUCs was significantly higher in MetS patients whose baseline TG concentration ≥ 1.7 mmol/l than the MetS cases whose baseline TG concentration was <1.7 mmol/L (mean ± SD in mmol*h/l = 34.36 ± 12.21 vs. 20.45 ± 7.91, P<0.0001, respectively). A schematic presentation of AUCs for TG in patients with MetS+veTG & MetS-veTG is shown in figure 3.

Linear regression analysis:-

Linear regression analysis was performed between the postprandial TG and fasting biochemical variables of metabolic syndrome. The post prandial TG was the dependent variables and Age, WC, BMI, BP, and fasting TC, TG, HDL-C, LDL-C, VLDL, Insulin, HOMA were independent variables, revealed that only TC, TG, VLDL, LDL were positively correlated and only fasting TG and VLDL showed significant (p<0.0001) correlation, while HDL-C showed insignificant inverse relationship with AUC for TG (figure 4).

DISCUSSION:-

In present study we assessed the presence of postprandial lipemia in Indian population with Metabolic syndrome. It was observed that metabolic syndrome patients had higher fasting and postprandial (table 1 & 2) responses during the OFTT (figure 1) and area under the curve (AUCs). We found that patients with higher fasting TG concentrations had greater postprandial response and higher AUCs than those with the lower TG levels. In metabolic cases AUCs was significantly higher than in the control subjects and fasting TG concentration was the strongest determinant of postprandial lipemia. Study supported by another study postprandial hyperlipidaemia may be a predictor of vascular risk [20]. They showed that men had greater plasma TG response 8 h after the fat load (284+/-117 versus 224+/-126 mg/dl, P=0.029). Only fasting TG levels significantly predicted the TG area under the curve (AUC) and incremental AUC. So postprandial hypertriglyceridaemia and seem to have delayed TG clearance.

Occurence of postprandial lipemia has been demonstrated in healthy people in different studies. In 2003, So et.al [21] have characterized patterns of lipid profile changes postprandially in healthy Filipino volunteers after oral fat challenge test (OFCT) with varied percentages of fat content (40% oral fat challenge test (OFCT), 45% OFCT, 50% OFCT). The study showed that triglyceride levels have increased to peak levels up to 274 to 310 mg/dl at median time of 4 to 5 hours after a high fat meal. In present study showed that triglyceride levels had increased to peak level from baseline at time 6 hours after the fat load in metabolic syndrome cases [figure 1.1]. Additionally LDL showed a decreasing pattern postprandially [22,23]. The elevated postprandial triglyceride levels may reflect a decrease clearance of triglycerides rich particles which can lead to further accumulation of these atherogenic particles [24].

Several biological mechanism gave explanation for the association between postprandial triglyceride levels and metabolic syndrome than cardiovascular disease. High fat food consumption, triglycerides are transported from the small intestine via chylomicrons through the bloodstream. Lipolysis of the triglycerides within chylomicrons,

catalyzed by lipoprotein lipase in tissues, transforms these particles into atherogenic, triglyceride rich remnant lipoproteins. An elevated postprandial triglyceride level, reflecting either a higher peak level or a delay in clearance of triglyceride-rich particles, can lead to an accumulation of these atherogenic particles [25]. It was noted in the present study that TG concentrations increases gradually during OFTT, but HDL-C and LDL-C levels decreased slightly, but not significantly at each base point from baseline [Table 2]. This results supported by Hyson D et al. [26] Mechanistic studies demonstrated that triglyceride-rich lipoprotein remnants may have adverse effects on endothelium and can penetrate into the sub endothelial space. Exchange of core lipids between postprandial lipoproteins and low-density lipoprotein (LDL)/high-density lipoprotein (HDL) is increased during prolonged lipemia, resulting in reduced HDL cholesterol levels.

In fact, large population studies (e.g. Women's Health Study and the Copenhagen City Heart Study) have assessed the association between non-fasting triglycerides and the risk of cardiovascular disease (CVD) events. It showed that increasing levels of non fasting triglyceride were associated with increased risk of MI, IHD and consequently death in men and women. Their finding propose that every 1 mmol/L increase in non fasting triglyceride levels correspond to further increase in the hazard ratio of the cardiovascular outcomes [27]. Borge G. et.al [28] also reported that non-fasting triglycerides ≥5 mmol/L vs. < 1 mmol/L marked a 17 and 5 fold increased risk of myocardial infarction, a 5 and 3 fold increased risk of ischemic stroke, and a 4 and 2 fold increased risk of early death in women and men in the general population. As all cells can degrade triglycerides it is biologically unlikely that it is the triglyceride molecules themselves that cause atherosclerosis and cardiovascular disease. Stalenhoef AF et al. [29] reported that the fasting triglycerides increase the adjusted hazard ratios for cardiovascular disease risk 1.7 x (comparing upper with lower tertile), and nonfasting levels around 2.0 x. Measurement of non fasting triglycerides may be more feasible and more informative.

In our study metabolic syndrome patients showed gradually increased significant postprandial values of TG and VLDL after 2hours and 4hours from fasting time. These levels peaked at 5-6hours after fat load and showed the gradually significant increased values than the fasting during 8 hours of observation [table 2 & figure 1.1 & 1.2]. It was observed that TG and VLDL area under curve were significantly increased in metabolic syndrome cases than control group (TG AUCs 27.2±9.51 vs 21.96±7.12 mmol*h/L; p<0.001) (figure 2) and (VLDL AUCs 5.4±2.81 vs 4.37±2.06 mmol*h/L; p<0.001). Present study supported by the Umpaichitra V et al. [30] reported, triglyceride AUCs was significantly greater in the diabetes group than in the other two groups (15.7 +/- 2.9 vs 9.2 +/- 0.7 and 7.5 +/- 0.7 mmol x h/l [1389 +/- 258 vs 819 +/- 60 and 663 +/- 62 mg x h/dl]; p < 0.02 and <0.004, respectively), as were insulin, C-peptide, and glucose AUCs. Incremental triglyceride response (delta triglyceride = peak - fasting) in the diabetic group was significantly higher than that in the control group (2.1 +/- 0.7 vs 0.8 +/- 0.1 mmol/l 189.7 +/- 58.4 vs 71.2 +/- 11.1 mg/dl]; p < 0.04). And the insulin resistance was greater in the diabetic group than in the obese and control groups (14.4 +/- 2.8 vs 5.2 +/- 0.8 and 3.2 +/- 0.4; p < 0.001 and < 0.0001, respectively).

In the present study all the TG and VLDL values were gradually significantly increased than the baseline values and found similar pattern. However, there is still a lack of data regarding VLDL values. Although in our analysis, VLDL had a significant postprandial rise and is considered as a component of postprandial lipemia as well. Samson et.al [31] had shown that patients with CVD have a prolonged postprandial lipemia compared to healthy individuals. He found the significant repeated, or the sustained postprandial increase, of the postprandial TG and VLDL levels shown in the study are also of significant importance. All the postprandial TG values up to the 12th hours of observation were significantly higher than the baseline at a range of 23.86 to 72.02 mg/dl (0.27-0.82 mmol/L). Thereby a similar pattern has been observed for VLDL. Different studies have shown that long duration of PPL and repetition of meals during daytime leads to a hazardous postprandial lipemia in metabolic and diabetic cases [26][32]. Such that prolonged lipemia leads to an increased opportunity for transfer of core lipids between the TRLs and HDL. This combination of high plasma TG concentrations, increased sdLDL and low HDL are known as the lipid triad or atherogenic lipoprotein profile.

In the present study postprandial responses were also during the OFTT in patients with MetS and baseline TG concentration either ≥1.7mmol/L (≥150mg/dl) (MetS+ve TG) or <1.7 mmol/L (<150 mg/dl) (MetS-ve TG), and control subjects are shown the table 3. Mean TG concentrations were significantly increased in the MetS+veTG patients compared with the MetS-veTG patients, and also in the MetS+veTG patients compared with the control subjects at all time points (0h, p<0.0001; 2h, 4h, 6h, and 8h p<0.001). In patients with MetS and baseline TG concentrations ≥1.7 mmol/L, AUCs was significantly higher than in MetS patients whose baseline TG concentrations were <1.7 mmol/L (Mean ± SD in mmol*h/L = 34.36±12.21 vs 20.45±7.91, p<0.0001). A schematic presentation of AUCs in patients with MetS+veTG and MetS-veTG is shown in figure 3. Present study results supported by Ntyintyane LM et al. [33] reported black CAD patients with and without MetS had similar fasting lipid profiles, postprandial responses during OFTT and AUCs. MetS patients with fasting TG > or = 1.7 mmol/l had greater postprandial responses (P < 0.001) and higher AUC (P < 0.0001) than patients with TG < 1.7 mmol/l. AUCs was higher in all patients than controls (P < 0.03). The most significant correlation was between fasting TG and AUC (r = 0.8703; P < 0.0001) and glucose (r= 0.4038;p<0.01). Other studies [34] also showed the postprandial response was significantly higher in MetS compared to HTN and healthy men [AUC (SD) in mg/dl/h; 2534 +/- 1016 vs. 1620 +/- 494 and 1019 +/- 280, respectively, p < or = 0.001]. The TG levels were increased significantly in MetS+TG compared to MetS-TG subjects at 4 (p = 0.022), 6 (p < 0.001) and 8 hours (p < 0.001). The TG were increased significantly in MetS-TG compared to healthy subjects at 4 (p = 0.011), 6 (p = 0.001) and 8 hours (p = 0.015). In linear regression analysis only fasting TG levels were a significant predictor of the AUCs (Coefficient B = 8.462, p < 0.001). The present study AUCs of TG showed the positive linear regression with BMI,WC, Glucose, TC, LDL,HOMA, Insulin and TG, VLDL, but significant correlation with fasting TG and VLDL (p<0.0001) while negative insignificant inverse correlation with HDL-C (figure 4).

In the present study the fasting insulin levels and its resistance (HOMA) were found significantly (p<0.0001) higher in metabolic cases. This results supported by the study of Christoph H et.al [35] observed both the MetS and insulin resistance predicted vascular events after controlling for non MetS risk factors [hazard ratio (HR), 2.74 (95% CI, 1.71-4.39; P <0.001) and 1.51 (1.24-1.84; P<0.001), respectively]. After additional adjustment for insulin resistance, the MetS remained significantly predictive of vascular events [HR, 2.69 (1.57-4.64); P<0.001], and conversely, insulin resistance remained significantly predictive of vascular events despite adjustment for the MetS [standardized HR, 1.41 (1.14-1.75); P= 0.002]. Additional adjustment for the presence of type 2 diabetes revealed that both the MetS [adjusted HR, 2.57 (1.47-4.51); P=0.001] and homeostasis model assessment of insulin resistance [standardized adjusted HR, 1.37 (1.09-1.73); P=0.007] significantly predicted vascular events independent from diabetes status.

Several studies supported the broad hypothesis that atherosclerosis is, at least in part, a postprandial phenomenon. Along with the possibly direct atherogenic effects of postprandial lipids, several established cardiac risk factors are associated with triglyceride levels. In particular, high levels are one manifestation of the constellation of metabolic disturbances associated with insulin resistance and the metabolic syndrome. Elevated postprandial levels of triglycerides may represent an abnormal response to an oral fat load due to insulin resistance, a hypothesis supported by previous case control studies in individuals with diabetes mellitus or the metabolic syndrome [36].

CONCLUSION:-

We concluded from the present study that fasting TG concentration is the main determinant of postprandial lipemia, because we found significant postprandial hypertriglyceridemia and significant delay in postprandial triglyceride clearance followed by standrized fat load in metabolic syndrome patients. These observation supported the conclusion that nonfasting triglyceride levels delivered to the liver by chylomicron remnants and may then be reassembled and returned to the blood in VLDL and reflects its level or remnant lipoprotein concentration than fasting triglyceride level. The higher predictive values of non fasting TG concentration for cardiovascular events have been proved directly by the postprandial increased concentration of chylomicrons, VLDL and their respective triglyceride rich remnants. Therefore, non fasting TG measurements performed in 4-6 hours after

fat load intake could replace direct measurement of the remnant lipoproteins for assessment of cardiovascular disease. The remnants of TG rich lipoproteins accumulated in the postprandial state are involved in atherogenesis. Thus clinician should be more affirm in addressing postprandial lipemia in this type of patients.

Most of the persons spent 24 hours in day in the non fasting state which especially considering the fact that TG may take up to 12 hours to return to fasting levels after meal. In Metabolic syndrome cases most of the persons already have the increased triglycerides level and according to the present data they will show the delay clearance of triglycerides and VLDL, that may be atherogenic. If postprandial triglycerides are biologically active in atherogenesis, measurement of fasting levels may provide insufficient information of atherosclerosis risk. Non fasting TG assessment may better predict CVD risk. Treatment guidelines should consider to include non fasting TG in their risk assessments.

ACKNOWLEDGMENTS:-
The author acknowledges the Research Centre and the subjects who participated in the study.

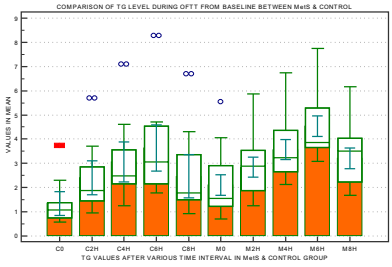

Figure 1.1 Comparison of TG values after various time interval in MetS and Control group

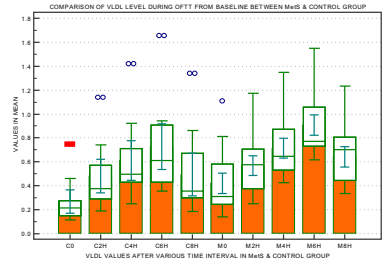

Figure 1.2 Comparison of VLDL level after various time interval in MetS and control group

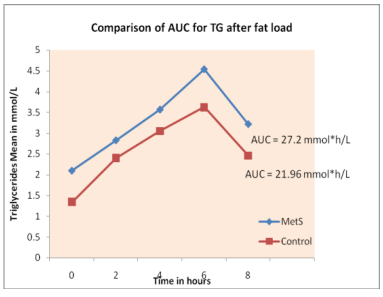

Figure 2 Comparison of AUC for TG after fat load in MetS & Control

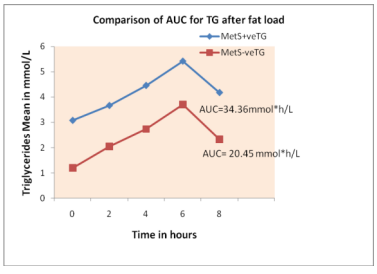

Figure : 3 Comparison of AUC for TG after fat load in MetS+veTG & MetS-veTG group

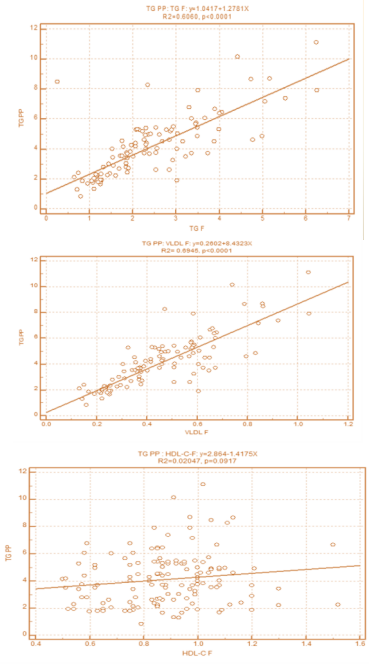

Figure :4 Linear regression graph of Metabolic patients TG AUC showing positive correlation with fasting TG (r = 0.6060;p<0.0001), fasting VLDL

(r = 0.6945;p<0.0001) and inverse insignificant correlation with HDL-C
® = - 0.02047;p=0.0917)

REFERENCES

1. Reaven GM, Banting L. Role of insulin resistance in human disease. Diabetes. 1988;37:1597-1607.
2. Meigs JB. Invited Commentary: Insulin resistance syndrome? Syndrome X? Multiple metabolic syndrome? A syndrome at all? Factor analysis reveals patterns in the fabric of correlated metabolic risk factors. Am J Epidemiol 2000;152:908-911.
3. Lakka HM, Laaksonen DE, Lakk TA, Niskanen LK, Kumpusalo E, Tuomilehto J, Salomen JT. The metabolic syndrome and total and cardiovascular disease mortality in middle aged men. JAMA 2002;288:2709-2716.
4. Fraser R. The role of dietary triglycerides in cholesterol metabolism. Atherosclerosis 1974;19:327-36.
5. Schrezenmeir, Fenselau S, Keppler I, Abel J, Orth B, Laue C et.al. Postprandial triglyceride high response and the metabolic syndrome. Am N Y Acad Sci 1997;827:353-68.
6. Adiels M, Olofsson SO, Taskinen MR, Boren J. Overproduction of very low-density lipoproteins is the hallmark of the dyslipidemia in the metabolic syndrome. Arterioscler Thromb Vasc Biol 2008;28(7):1225-1236.
7. Schaefer EJ, McNamara JR, Tayler T, Daly JA, Gleason JA, Seman LJ et.al. Effects of Atorvastatin on fasting and postprandial lipoprotein subclasses in coronary heart disease patients versus control subjects. Am J Cardiol 2002;90:689-696.
8. Lewis GF, Meara O NM, Soltys PA et.al. Fasting hypertriglyceridemia in non insulin dependent diabetes mellitus is an important predictor of postprandial lipid and lipoprotein abnormalities. Journal of Clinical Endocrinology and Metabolisms 1991;72(4):934-944.
9. Lairon D and Defoort C. Effects of nutrients on postprandial lipemia. Current Vascular Pharmacology 2011;9(3):309-312.
10. Bravo E, Napolitano M and Botham KM. Postprandial lipid metabolism: the missing link between life style habits and the increasing incidence of metabolic disease in Western Countries? Open Translational Medicine Journal 2010;2:1-13.
11. Mottillo S, Filion KB, Genest J et.al. The metabolic syndrome and cardiovascular risk: a systematic review and meta analysis. Journal of the American College of Cardiology 2010;56(14):1113-1132.
12. Expert panel on Detection, Evaluation and treatment of high blood cholesterol in adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP III). Journal of American Medical Association (JAMA) 2001;285(19):2486-97.
13. Patsch JR, Karlin JB, Scott LW, Smith LC, Gotto AM Jr. Inverse relationship between blood levels of high density lipoprotein sub fraction 2 and magnitude of postprandial lipemia. Proc Natl Acad Sci USA 1983;80:1449-53.
14. Berthelot, M.P.E., Report Clin. Appl. 2884 (1859).
15. Bowers L.D., Clin. Chem., 26, p 551-556 (1980).
16. Trivedi R.C., et. al., Clin. Chem., 24(11), 1908-1911 (1978).
17. Trinder, P. Ann.Clin.Biochem 6:24 (1964).
18. Tsao TS. ACRP30 a new hormone controlling fat and glucose metabolism. European Journal of Pharmacology, 440(2-3):213-221(2002).
19. Matthews JNS, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. Br Med J 1990;300:230-35.
20. Kolovou GD, Anagnostopoulou KK, Pavlidis AN, Salpea KD, Iraklianou SA, Hoursalas IS, Mikhailidis DP, Cokkinos DV. Eur J Cardio Vasc Prev Pehabil 2006 13(4):661-4.
21. So T, Mercado Asis L, Zacarias M. A Comparison of Dose Response Postprandial Lipid Profile of Healthy Filipino Subjects after an oral fat Challenge Test of Varying Fat Contents. Phill J Internal Medicine 2004;42:1-7.
22. Tsunoda F, Koba S, Hirano T, Ban Y, Iso Y, Suzuki H, Geshi E, Katagiri T. Association between small dense low-density lipoprotein and postprandial accumulation of

triglyceride-rich remnant-like particles in normotriglyceridemic patients with myocardial infarction. Circ J Dec 2004;68(12):1165-72.
23. Takayanagi N, Onuma T, Kato S, Nishiyama K, Nomiyama T, Kawamori R. Association between LDL particle size and postprandial increase of remnant-like particles in Japanese type 2 diabetic patients. Diabetes Res Clin Pract Dec 2004;66(3):245-52.
24. Ginsberg HN. New perspectives on atherogenesis role of abnormal triglyceride rich lipoprotein metabolism. Circulation 2002;106(16):2137-42.
25. Opie LH, Mayosi BM. Cardiovascular disease in sub Saharan Africa. Circulation 2005;112:3536-40.
26. Hyson D, Rutledge JC, Berglund L. Postprandial lipemia and cardiovascular disease. Curr Atheroscler Rep Nov2003;5(6):437-44.
27. Nordestgaard BG, Benn M, Schnohr P, Tybjaerg Hansen A. Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease and death in men and women. JAMA 2007;298(3):299-308.
28. Shojee-Moradie Fariba, Yuying Ma, Shaoying Lau, Roman Hovarka and Umplesy Margot A. Prandial hypertriglyceridemia in metabolic syndrome is due to an overproduction of both chylomicron and VLDL triacylglycerol. Diabetes Dec 2013;62:4063-4069.
29. Stalenhoef AF, de Graaf J. Association of fasting and nonfasting serum triglycerides with cardiovascular disease and the role of remnant-like lipoproteins and small dense LDL. Curr Opin Lipidol. Aug2008;19(4):355-61.
30. 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. Jun2004;17(6):853-64.
31. Samson E, Ana Lyza, Galia B, Khristine Ivy C Llave, Manuel B. Zacarias, Leilani B. Mercado Asis. Postprandial peaking and plateauing of triglycerides and VLDL in patients with underlying cardiovascular disease despite treatment. Int J Endocrinol Metab 2012;10(4):587-593.
32. Scott M Grundy. Atherogenic dyslipidemia associated with metabolic syndrome and insulin resistance. Clinical cornerstone 2006;8(1):S21-S27.
33. Ntyintyane LM, Panz VR, Raal FJ, Gill GV. Postprandial lipaemia, metabolic syndrome and LDL particle size in urbanised South African blacks with and without coronary artery disease. QJM Feb2008;101(2):111-9.
34. Kolovou D Genovefa, Anagnostopoulou K Katherine, Pavlidis N Antonis, Salpea D Klelia, Iraklianou A Stella, Tsarpalis Konstantinos, Damaskos S Dimitris, Manolis Athanasios and Cokkinos V Dennis. Postprandial lipemia in men with metabolic syndrome, hypertensives and healthy subjects. Lipids in Health and Disease 2005;4:21.
35. Christoph H Saely, Stefen Aczel, Thomas Maste, Peter Langer, Guenter Hoefle and Heing Drexel. The Metabolic syndrome, insulin resistance and cardiovascular risk in Diabetic and non diabetic patients. Journal of Clinical Endocrinology & Metabolism, 90(10):5698-5703.
36. Ginsberg HN. Insulin resistance and cardiovascular disease. Journal of Clinical Investigation 2000;106(4):453-458.