DISCUSSION
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Diabetes mellitus is one of the important secondary causes of hyperlipidemia and almost every diabetic sooner or later appears to have enough lipids to develop atherosclerosis under the right circumstances and local factors play a decisive role as to whether and where they will form.

In the present study 22 diabetics both type-1 (8 cases) and type-2 (14 cases) were in basal state (I) 7 days after high cholesterol fat breakfast (HCFB) (14 cases) and 7 days after withdrawal of HCFB and 8 cases at 1 hr and 3 hrs to study the changes in lipid profile.

A. PROLONGED FEEDING

1. SERUM TOTAL CHOLESTEROL (STC)

Seven days after HCFB there was an increase in STC. In type-1 diabetics all the cases (100%) showed an increase after HCFB. In type-2 diabetics 6 cases (66.67%) showed arising pattern but in 3 cases (33.33%) a fall in STC was observed after feeding.

Amelioration of lipemia during treatment with high fat diets had been reported by Cowie (1921) and Marsh et al (1923). Though exact mechanism is not described by them. After all why then is a fall after feeding of HCFB in substantial minority ?
The rise in STC after HCFB is suggestive of diet induced hypercholesterolemia. This increase in STC may be because of either:

a. Mobilization of cholesterol from the tissue (indicates in the form of HDL rise). In our study there is a rise in HDL after feeding as shown in table 17 & 18).

b. Stimulation of endogenous synthesis of cholesterol.

c. Inability of body (enzyme or liver) to utilise the acutely increased cholesterol because of excessive absorption.

d. Defective excretion of absorbed cholesterol.

Seven days after withdrawal of diet 3(60%) cases of type-1 and 7(77.77%) cases of type-2 showed a fall in STC level. Yet 2(40%) cases of type-1 and 1(11.11%) case of type-2 showed a further rise in STC. It may be probably because of uninterrupted stimulation of endogenous cholesterol synthesis.

In one case (No. 7) of type-2 diabetic, the STC level remained same even after withdrawal of diet.

The basal level of STC were higher in smokers (type-1 and type-2). 7 days after HCFB the increase in STC was lower in smoker than non-smokers. This finding is in accordance with Konttinen and Rajasalmi (1963).

There was no significant differences in STC levels between vegetarian and occasional non-vegetarians, alcoholics and nonalcoholics. Probably it could be because of the frequency (as little as once in a week) of meat intake and alcohol once in a blue moon was
insufficient to produce any change.

Highly significant difference was observed between consumers of high fat and low fat in their usual diet in our study (type-1 diabetics). In type-2 diabetics the STC level was insignificantly higher. In healthy individuals (high fat consumers) higher level of STC was observed by Keys et al (1961); Brontestewart (1958) and Hegstest et al (1965). However, Page et al (1965) observed no significant relationship between dietary cholesterol and STC levels.

Similarly uncontrolled diabetic had higher level of STC both in type-1 and type-2. Lewis et al (1972) have shown that treatment of diabetic patients with insulin reduces free fatty acid concentration, but the levels are still higher than in controls. However, Shapiro et al (1973) in a study of cholesterol and triglyceride in white and Bantu showed that treatment with insulin did not have significant effect in lowering lipids in white population.

2. **CHANGES IN HIGH DENSITY LIPOPROTEIN (HDL)**

The basal level of HDL in type-1 diabetics (36.66±10.64 mg/dl) and type-2 diabetics (50.45±22.83 mg/dl) were lower than controls (45.00±19.78 mg/dl and 60.66±21.18 mg/dl respectively).

In type-2 diabetics plasma HDL cholesterol level tends to be decreased (Calvert et al, 1978). Lower level of HDL in diabetics were also observed by Barbara et al
Seven cases of type-2 diabetic (77.78%) and all cases (100%) in type-1 diabetics showed an increase in HDL. So overall 85.71% cases showed an increase in HDL after feeding. Only in 12.28% cases a fall in HDL was observed following 7 days after HCFB. This rise in HDL could be because of increased synthesis of HDL.

In 12.28% cases, in whom initially a fall in HDL was observed after feeding they showed an increase in HDL following withdrawal of diet. This could be because of transient inhibition of HDL synthesis. Low level of HDL in type-1 diabetics, who were smokers was observed as compared to non-smokers. Reduction in HDL have been observed after smoking by Bierman (1983).

Surprisingly a high level of HDL in smokers (type-2) were observed. We can not offer an explanation for this paradoxical findings. No significant difference in serum HDL was observed in nonvegetarians, alcoholics, high fat consumers type-1 and type-2 diabetics when compared with respective vegetarian, nonalcoholics and low fat consumers in diet. This could be because of the level of meat intake and alcohol consumption was insufficient to produce any significant change.

The patients whose blood sugar were well controlled (type-1) were having higher level of HDL. It has been suggested that insulin treatment raises HDL. Levels in patients with type-1 diabetes (Mikkila, 1981).
3. **CHANGE IN LOW DENSITY LIPOPROTEIN (LDL)**

The basal level of serum LDL in type-1 diabetics (104.32±37.37) and in type-2 diabetics (140.20±32.6 mg/dl) were higher than respective controls (89.05±33.53 and 100.53±29.79 mg/dl).

High level of basal LDL have also been reported by Barbarav, Howard et al (1978) and Simpson et al (1979) in diabetics.

Four (80%) cases of type-1 and 4 (44.4%) cases of type-2 diabetics showed an increase in LDL after HCFB, whereas 1 case of type-1 and 5 (55.6%) cases of type-2 diabetics showed a slight fall after HCFB. So overall 57.14% cases showed an increase in LDL after feeding whereas a 42.85% cases a fall was observed after feeding. After withdrawal of diet 64.28% cases showed a fall in LDL but in substantial minority 35.71% cases further rise was observed.

Again smokers have higher level of LDL in type-1 (106.15±53.23) and in type-2 diabetics (145.20±39.90 mg/dl) as compared to non smokers of same group. Smoking is one of the predisposing factor for atherosclerosis and higher level of LDL is a well known atherogenic.

The patients who were consuming high fat in diet were having significantly higher level of LDL in both type-1 and type-2 diabetics when compared with patients who were consuming low fat in diet. There were no significant differences in LDL level in non vegetarian
and alcoholics when compared with vegetarians and non-alcoholic diabetics. This could be probably because of very small amount of alcohol used and meat hardly weekly.

The LDL levels in uncontrolled diabetics (type-1 and type-2) were higher than the patients whose blood sugar were well controlled. Higher level of LDL in untreated diabetics were also observed by Ballantyne et al (1977) in type-2 and Dunn (1981) in type-1 diabetics.

The exact mechanism is not yet clear but it could be because of:

1. VLDL is the major precursor for LDL in plasma and increased synthesis of VLDL in diabetes leads to increased formation of LDL.

2. There is decreased catabolism of LDL in poorly controlled diabetes because of a decreased ability to LDL to interact with in cell surface receptor (Witsman, 1982). The decreased catabolism of LDL appears to be due to glycosylation of plasma LDL (Witsman, 1982) which alters the configuration of LDL so that it is less able to interact with specific LDL receptors responsible for majority of LDL catabolism in normal individuals (Brown et al, 1982).

4. **Changes in Serum Triglyceride and VLDL**

Higher basal level of STG were observed in type-1 diabetics (205.68±34.71 mg/dl) as compared to normal subjects (129.75±19.88). Similarly type-2
diabetics were also having (215.16±28.15 mg/dl) higher values of basal STG.

Since VLDL is just one fifth of the STG so higher level of VLDL was also observed in type-1 (41.13±7.34 mg/dl) and type-2 diabetics (43.14±5.61) as compared to normal individuals (26.39±3.44 mg/dl and 16.47±2.24 mg/dl respectively).

Higher level of STG and VLDL in diabetics have also been reported by many researchers like Barbara, V. Howard (1983); Kissebah et al (1982); Greenfield (1980) and Abrams (1982).

There may be two possible mechanisms for the increase of VLDL in type-2 diabetics. A clearance defect has been postulated with a decreased fractional catabolic rate for VLDL triglycerides (Brunzell et al, 1979). It is known that lipoprotein lipase is under hormonal regulation by insulin (Borensztain et al, 1972) and the activity of the enzyme has been shown to be reduced in adipose tissue and muscles in uncontrolled diabetes (Taskinen et al, 1982).

Further more there are increased synthesis of VLDL-TG by the liver (Dunn et al, 1980) in type-2 diabetes.

In type-1 diabetics there is acute deficiency of insulin which results in a rapid increase in both free fatty acid mobilisation from adipose tissue and secretion of VLDL and ketone bodies from liver (Balasse, 1972).
Clearance of triglycerides from the plasma is also impaired. The later effect is thought to be the result of decreased activity of the enzyme lipoprotein lipase (Fielding, 1972) which requires the presence of insulin for maintenance of adequate tissue level (Pykalisto, 1979).

We could not establish any definite significant relationship between STG or VLDL in alcoholics/nonalcoholics, vegetarians/nonvegetarians, low/high fat consumers and smoker/non-smokers.

Basal STG and VLDL levels were higher in uncontrolled diabetics as compared to the patients whose blood sugar were controlled.

The patients who were taking oral hypoglycemics alone (type-2) were having higher level of STG and VLDL than the patients who were taking both oral hypoglycemics and insulin. Lewis et al (1972) have shown that STG were also reduced by insulin. However, Shapiro et al (1973) showed that in white and Bantu there was a trend of reduced STG.

B. SINGLE DOSE FEEDING

1. CHANGE IN STC

In type-1 diabetics 100% cases showed an increase in the level of STC at 1st and 3rd hrs. But in type-2 diabetics in 2(40%) cases rise in STC was observed at 1 hr followed by a fall at 3 hrs. In 3(60%) cases a slight fall at 1 hr and 3 hrs was observed.
2. **CHANGE IN HDL**

   In 4 (50%) cases an increase in HDL at 1 hr was found followed by a fall in the same cases at 3 hr.

   Two (25%) cases showed slight fall at 1 hr was found whereas in another 2 cases it remained same followed by a fall at 3 hrs.

3. **CHANGE IN LDL**

   Type-1 diabetics all cases (100%) showed a gradual rise in LDL level at 1 hr and 3 hrs but in type-2 diabetics only 1 (20%) case showed an increase in LDL at 1 hr. Rest in 80% cases a fall at 1 hr was found. At 3 hr in 2 (40%) cases a further fall was observed but in another 2 cases an increase was observed at 3 hrs.

4. **CHANGE IN VLDL AND SERUM TRIGLYCERIDE**

   All type-2 diabetics showed an increase in STG and VLDL at 1 hr. In 3 (60%) cases a further rise in STG was seen at 3 hrs whereas in 2 (40%) cases rise in STG was followed by a fall.

   In type-1 diabetics 2 (66%) cases an increase in STG was observed at 3 hrs but in 1 case a slight fall was observed at 3 hrs.

   Katam (1983) held that three factors influence the effect of dietary cholesterol on serum cholesterol in human beings:

1. Composition of the diet with respect to other nutrients including polyunsaturated fatty acids and unknown anti or prohypercholesterolemic agents.
2. The baseline level of dietary cholesterol from which observations are made and

3. Individual variability: some peoples are hyperresponders and some are hyporesponders.

Basically after feeding the various lipoprotein fractions show 3 types of responses. In a majority of cases cholesterol feeding causes an increase of plasma cholesterol and its various subfractions but in substantial minority feeding causes either a decrease or no change in lipoproteins. Similarly after withdrawal of HCPB the majority show a decline in the serum lipoproteins including cholesterol but again a substantial minority does not show any change or shows an actual increase from post feeding values.

Why in some cases cholesterol and in subfractions decrease after feeding and further increase after withdrawal is a question that has not been satisfactorily explained. We offer no explanation.

Further work is needed to explain these findings.