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Diet Heart Hypothesis– Review

Dr.Kanase C.A.
MBBS, MD,
PhD scholar.
HOD practice of medicine at AKHMC, Alephata

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There are essential amino acids (proteins) and essential fatty acids (fats) - which we must eat. Deficiency of these essential ingredients will lead to deficiency disorders. But there are no essential carbohydrates and there are no carbohydrate deficiency disorders. Carbs (non essential) constitutes a major component of daily meal (especially in India). Carbs are recommended to be the important part of daily meal. There are variety of dietary manipulations advised for managing Type 2 DM / Insulin resistance.

Dietary carbohydrates are known to increase postprandial plasma glucose, triglycerides and insulin. Since long dietary carbs areconsidered as obesogenic due to their impact on insulin secretion(1)(2). If you try to reduce any one macronutrient, automatically you have to increase some other macronutrient. If you reduce carbohydrates you have to increase either proteins or fat.

What is the exact nature of problem?- Commonly it is believed that dietary cholesterol, saturated fat consumption leads to increase in serum cholesterol / LDL.Which further leads to atherosclerotic cardiovascular diseases - ASCVD. This ultimately leads to increased prevalence and incidence of IHD, stroke and peripheral vascular disease. The hypothesis was proposed by Dr Ancel Keys in 1952.It was later followed by his famous 7 country study(3) in 1958. There are various arguments about this study (4). The study is endorsed and condemned by various researchers in future.

So as to decrease the problem of ASCVD, peoples are being advised to lowerthe dietary calories, cholesterol and saturated fatconsumption. The serum cholesterol should be reduced further with the help of drugs – statins, PCSK 9 inhibitors. So ultimately the dietary cholesterol, saturated fatsare vilified. The issue started with the introduction of first dietary guidelines in 1980(5).

Whether the guidelines are being followed? –The dietary guidelines are accepted and implemented all over the world. Fat consumption is decreased with increase in sugar and refined carb consumption (4).

Should the guidelines be need to be reviewed? - The guidelines are followed worldwide and in India(6). But since the dietary guidelines are implemented the ASCVD and chronic diseases like T2DM, obesity, hypertension, dislipidemia, PCOS, (insulin resistance) are seen in increasing proportions with clear upward trend from 1980(2)(7).

The guidelines apparently did not helped to control the situation(CVD) for which they were introduced.The guidelines are periodically being updated with little changes(8). Many researchers have questioned the usefulness, necessity and scientific background of the dietary recommendations (9).

Does Dietary cholesterol increase serum cholesterol? - Cholesterol is the most vital element of every cell. All the cells in the body (possibly except brain cells) can make cholesterol. Dietary cholesterol has very little impact on serum cholesterol about8 hours after meal(9).The dietary cholesterol is in esterified form and onlypartly absorbed in the proximal intestine.

Cholesterol homeostasis - If food intake of cholesterol is more,liver synthesizes less cholesterol andincreases biliary excretion of cholesterol. If dietary intake of cholesterol is low the less is excreted and more cholesterol is synthesized by the liver. The cholesterol is not broken down in the body. About 80 % of cholesterol is synthesized by the body itself. About 20% cholesterol is contributed by food sources.But important question is whether cholesterol is dangerous?Plant sterols are poorly absorbed and rapidly excreted and cannot be synthesized in the human beings(10).

Does increased serum cholesterol causes increased risk of CVD?- The recent epidemiological data analysis does not support the commonly believed theory that increased serum cholesterol causes heart disease(11). If serum cholesterol causes ASCVD then obviously the individuals with familial hypercholesterolemia

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should have shorter life span. But even the research in 1966 (before the dietary recommendations) clearly shows that familial hypercholesterolemia is not associated with shortening of life span of the individuals with this disorder(12)

The Honolulu heart program- (3572 Japanese individuals, 20year cohort study) has also concluded that–

- Long term low serum cholesterol is associated with increased risk of death (13)
- The risk of having ASCVD is higher after the age of 60. The cholesterol was found to be protective in this age group(13).
- The research raised serious questions about use of drugs to lower cholesterol especially in older individuals.

The Sydney Diet Heart Studyand updated meta analysis– In 2013 when the uncovered data from the Sydney diet heart study (conducted between 1966 and 1973) was analyzed, it was found that replacing saturated fat with linoleic acid resulted in slightly increased risk of allcause mortality(14).

The Minnesota Coronary Experiment – (9500 participants, randomized study). Saturated fat was replaced with linoleic acid. No benefits was found in linoleic acid group. Trial was conducted from 1968 to 1973. Results were not published till 1989. (15)

Minnesota coronary survey – 2016 – Additional and previously unpublished data from Minnesota coronary experiment was reviewed. Review confirmed that there is lack of association between saturated fat and CHD and risk of death. There was decrease in LDL cholesterol levels in linoleic acid group but was associated with marginally higher risk of CHD mortality. The researchers stated that this was likely dur to adverse metabolic changes from intake of linoleic acid a known inflammatory agent when consumed in high amount(15)

Prospective Urban Rural Epidemiology – (Nov 2017)–In this study it was found that higher saturated fat intake was associated with beneficial effects on cardiovascular risk factors like HDL, triglycerides, Apo B / Apo A (16). Even the additional 7 year follow up revealed no association between saturated fats and heart disease with decreased risk of all cause mortality and stroke.

MRFIT – Multiple Risk Factor Intervention Trial–This study is cited and quoted many times. It clearly states that serum cholesterol is directly proportional to CVD risk in the patients and was concluded – a 1% higher serum cholesterol level are associated with almost 2 % higher CHD risk(17).The conclusion is based on the relative risk ratio concluding over 400 %(4 times) death rate in those with highest serum cholesterol levels (more than 290 mg / dl) as compared to those with normal cholesterol levels (150 mg/dl). But actual raw data analysis shows that the absolute difference in mortality is only 1% which is small and statistically insignificant.

In 2016 a systematic review concluded that in elderly individuals with higher LDL is associated with better life span (18).The researchers also raised questions over validity of cholesterol hypothesis.

LDL cholesterol in particular is also considered to be atherogenic in nature. Variety of dietary interventions are also advocated for lowering serum cholesterol like corn oil (19). Corn oil was found to be successful in lowering the serum cholesterol but the mortality was significantly higher in intervention group (50% against 25 %)(20)

Does cholesterol lowering drugs really help in patients with CVD – (primary or secondary protection)? -

The lipid research clinics coronary primary prevention trial – 1984 This is the biggest trial with cholestyramine to reduce serum cholesterol. It showed 24 % benefit in CHD mortality in intervention group against the placebo(21). This was a relative risk benefit of 24 % against the absolute risk benefit of .4 % (1.6 % vs 2 %). The allcause mortality was observed to be not reduced significantly(21).

The statins are extensively studiedand are considered to have magical effects in preventing and managing the individuals with ASCVD. Obviously enough these studies are funded by the pharma majors – conflict of interest. Statins are claimed to have variety of mode of actions –

- restoring or improving endothelial function,
- attenuating vascular remodelling,
- inhibiting vascular inflammatory response,
- stabilizing atherosclerotic plaques.
- reducing cholesterol / LDL

JUPITAR trial –In an attempt to lower the cholesterol further statins were introduced. Atorvastatin and rosuvastatin both trials have usedsame tool (relative vs absolute risk) to artificially inflate the effectiveness of the drugs.The JUPITAR study statistics is as follows-Event free - Rosuvastatin – 98.4 %, Placebo – 97.2 %. Difference = 1.2 % - Absolute risk.Risk – Placebo

group has a 100 – 97.2 = 2.8 % risk.The relative risk reduction is = 1.2 % / 2.8 = 44 %. With NNT = 1/ ARR = 1/ 0.012 = 83

Anglo- Scandinavian cardiac outcome trial – ASCOT - Atorvastatin was claimed to be effective in lowering the risk of heart attack by 36 % (22).This is relative risk reduction. The absolute risk reduction was 1.1 % with NNT = 1/ ARR = 91.The trial was terminated prematurely.

What about dietary saturated fats and CVD risk?– Saturated fat is an important and major component (50%) of all the cell membranes in the body. The dietary recommendations are to restrict dietary saturated fat intake to less than 10 % of daily calorie intake(6). The saturated fat is known to increases LDL cholesterol. But this increase is in large particle LDL cholesterol. The small dense LDL is atherogenic once it is oxidised(23). Most of the meta analyses failed to show any beneficial effect of dietary saturated fat restriction on CVD and mortality(23). Actually the dietary saturated fat was found to have protective effect on stroke. The beneficial effects are assigned to other food ingredients(micronutrients, phospholipids, proteins, probiotics) in unprocessed foods. The ingredients added during processing are unhealthy. The researcher concluded that – The totality of available evidence does not support further limiting the intake of such foods (whole fat dairy, unprocessed meat).

Cardiovascular Health Study - A study involving 22 years of follow up actually showed protective effect with butter consumption in risk of stroke up to 42%(24).

Then what causes Heart disease?– The popular concept of cholesterol / saturated fat / LDL cholesterol causing heart disease is under scanner in various studies. Dr Aseem Malhotra and others have concluded that - saturated fat was observed to be actually protective in nature for ASCVD in primary prevention as well as secondary prevention of ASCVD. Carbohydrate and polyunsaturated fat intake found to have adverse association with progression of ASCVD(25).

Women's Health Study - In another trial - 28024 women participants over age 45 yr / 21.4 yr median follow up) Diabetes along with insulin resistance was found to be a major- 8 times- risk factor as against cholesterol, LDL(22).

Research with low carb diet - The low carb diet is studied across the world with encouraging results(27). The safety and efficacy of low carb diet is also verified in many studies (28)(29)(30). The low carb diet for managing type 2 DM is also shown to be sustainable and safe in many studies(31).The carbohydrate as a cause of hypertriglyceridemia is known since 1961. Serum levels of triglycerides are more responsive to dietary carbs than to dietary fats (32).

Research with processed food – The link between processed food consumption and type 2 DM is also observed in almost all the studies(30). All researchers across the world have insisted on quality of the food as an important determinant in public health and preventing and managing the type 2 DM and associated disorders(33).

What about Indian research with low carb diets?– The research about dietary intervention in the management of type 2 DM is mainly from USA and other countries (34).In India very little research work is done in the field of nutrition. India and other southeast countries use carbohydrates as the main food source in daily diet. India is already being projected as the DM capital of world. We in India need to verify the utility of the low carb diet in T2 DM management(35)**.** Another group of researchers have also demonstrated a improved biochemical output with low carb high protein diet(36). In another review article the author acknowledged that in South Asians, higher dietary carb intake leads to postprandial hyperglycaemia, hyperinsulinemia and hypertriglyceridemia and PUFA supplementation shows improvements in these parameters (37). In an another review the polished rice has been blamed for increasing prevalence of diabetes in India (38). All these researchers point towards high dietary carbs as the important contributor for diabetes in India. In another study the increased fat intake was observed to be associated with deranged parameters of metabolic syndrome (39)**.** The researchers themselves have referred to many confounders like increased sugar intake, smoking along with fat.

In summary –

- Dietary carbs are non essential.
- Carbs constitute the major form of calories in daily food for most of the South East Asians and Indians.
- There is no scientific evidence to support that the dietary cholesterol and saturated fat causes heart disease/ ASCVD(25).
- The effects of lowfat high carb diet do cause reduced levels of total and LDL cholesterol in plasma but does not lead to improved clinical outcome.

- The benefits of the cholesterol lowering drugs appear better due to data manipulations (actual risk vs relative risk).
- The drug trials are funded by pharma majors – conflict of interest.
- Replacing saturated fat with PUFA / MUFA does not offer any benefit.
- In case of ASCVD, diabetes along with insulin resistance is a strong (8 times) predictor of CVD than LDL cholesterol.
- Low carb dietary intervention is known to have beneficial effects in patients with Type 2 DM in lowering plasma glucose, insulin, triglycerides, reducing drug requirement and possibly can lead to remission in some patients.
- The research work from India is very minimal and mainly in the form of epidemiology studies.
- We need Indian study for effectiveness of low carbohydrate diet on glycaemic controlin patients with Type 2Dm in the form of randomised controlled clinical trial.

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