Correlation of Dietary Pattern and Risk Factors in Patients with Coronary Artery Disease in Rural Population of Tamil Nadu - Pilot Study

Authors
Dr A. G. Narayanaswamy1*, Dr P. Vinodh Kumar2, Dr S. Porchelvan3, S. Pavithra4
1Senior Consultant, Cardiology, Saveetha Medical College, Thandalam, Chennai 602105
2Assistant Professor, Cardiology, Saveetha Medical College, Thandalam, Chennai 602105
3Professor, Biostatistics, Saveetha Medical College, Thandalam, Chennai 602105
4Dietician, Saveetha Medical College, Thandalam, Chennai 602105
Corresponding Author
Dr A. G. Narayanaswamy
Department of Cardiology, Saveetha Medical College, Thandalam, Chennai – 602105
Telephone No: 9444054861, Email: agncard@yahoo.co.in

Abstract
Worldwide studies have reported increase in the incidence of CAD in illiterate & people with lower socio economic status1. Based on cross sectional morbidity surveys incidence of coronary heart disease has increased two fold, (2.06% is 1970's to 4.04% in 1990's) in rural India3. There is no published data correlating dietary pattern & risk factors in patient with CAD in rural Tamil Nadu.
Aim: Correlation of dietary pattern and risk factors in patient with CAD in rural Tamil Nadu.
Study Design: Retrospective case control study. All patients residing in rural areas who underwent CAG in our centre with evidence of CAD were enrolled for the study after informed consent.
Methodology: All the patients with CAD were interviewed by the dietician of our hospital regarding their diet pattern, using a 7days dietary recall questionnaire. This was analysed & daily intake fat, carbohydrates, protein & total calories of each patient was tabulated & compared with recommended dietary allowance 2010 guidelines for Indian (ICMR).
Results: A total of 148 patients who underwent CAG 39.9% (59 patients) had normal CAG, 29.1% (43 patients) had SVD, 17.6% (26 patients) had DVD and 13.5% (20 patients) had TVD. Male & Female patients were equally distributed in CAD & normal group (P=0.24). Patients with Hypertension (OR 1.4, 95% CI: 0.6 – 2.9), Diabetes (OR 1.85, 95% CI: 0.91 – 3.71) tended to have CAD, however it did not reach statistical significance. The mean intake of carbohydrates, protein, and fat did not reach statistically significance between the 2 groups. There was a significant difference in carbohydrate intake in patients with single vessel disease, but did not reach statistical significance in patients with double / triple vessel disease when compared with normal coronaries.
Conclusion: Risk of CAD in rural population of Tamil Nadu is not related to total carbohydrates or fat intake. Coronary artery disease could be related poor intake of vegetables and fruits.
Keywords: Coronary Artery Disease, Dietary Pattern, rural population.
Introduction
Studies from Europe and United States during the past 30 years has shown that the prevalence of coronary heart disease and coronary risk factors have increased in the illiterate and people of low socio economic status. As per the WHO reports cardiovascular deaths 20% cardiovascular deaths occur in the high income countries, 8% in upper-middle income countries, 35% in lower-middle income countries and 37% in low income countries. Reliable data about incidence of cardiovascular disease is not available in India since mortality data is scarce in India. Based on cross sectional morbidity surveys it has been found that the incidence of coronary heart disease in urban India has increased nine fold (1.04% in early 1960s to 9.45% in mid 1990s), whereas in rural India it has increased two fold (2.06% in 1970s to 4.04% in 1990s).

Socio economic status and coronary heart disease
Data from the Registrar general of India states that in 1998 the cardiovascular diseases contributed to 27% of deaths. There were major differences in the mortality rates among various states, with affluent states like Punjab, Andhra Pradesh and Tamil Nadu have significantly higher CV mortality rates compared to poorer central and eastern states. Among immigrant populations from rural to urban areas it was found that lower socioeconomic groups had significant risk factors for coronary artery disease in the form of tobacco use, increase in level of diabetes, reduced consumption of fruits and vegetables and psychosocial stress.

Nationwide studies are nonexistent. The Indian immigration study was the only study to include population from north, centre and south of India. Studies from rural India although from various states show that compared to the 1990s the population in 2000s have increased incidence of obesity, diabetes and hypercholesterolemia. Tobacco and alcohol use and low fruit and vegetable intake were more common in lower socioeconomic groups, whereas obesity and some of its related risk factors (dyslipidemia and diabetes in men and hypertension in women) were more common in higher socioeconomic groups. Tobacco and alcohol use were more common in men, while obesity and low intake of fruits and vegetables were more common in women. Risk factors were more prevalent among south Indians compared with north Indians.

Chadha et al (1997) performed a community-based survey of coronary heart disease and its risk factors in Delhi and its adjoining rural areas. The overall prevalence of coronary heart disease among adults based on the clinical and ECG criteria was estimated as 9.7% and 2.7% in the urban and rural populations, respectively. There was highly significantly higher prevalence in the major risk factors in urban versus rural population. In 2011, a large population survey from rural and urban samples of three geographical regions of Kerala was conducted. The study showed an alarming increase in the prevalence of CAD and most of the major risk factors. The study showed that the prevalence of CAD in Kerala has risen over the past two decades, mainly driven by the rise in coronary risk factors. There was a high prevalence of CAD among young individuals (2%) as compared to western data (1.2%). Contrary to most of the previous Indian data, there was no difference between urban (15.1%) and rural (16.2%) prevalence of CAD in this study.

Methodology and Research Design
It is a case control study. All patients from rural areas, who underwent CAG at our centre, with evidence of CAD, were enrolled for the study after informed consent. Patients were enrolled for the study, after informed consent if they satisfied the criteria for residence in rural area as per 2011 census guidelines and National Sample Survey Organisation (NSSO).

Modified Kuppusamy Scale (corrected for the current year using consumer price index) was used for assessing their socio economic status. Anthropometric measurements including, height,
weight, waist hip ratio and height to waist ratio were measured.

**Risk factors studied were**
- DM – Diagnosed as per guidelines (ADA 2016 guidelines); whether on treatment or not; on insulin or OHAs
- Hypertension – Diagnosed as per guidelines (JNC 7 guidelines); drugs used.
- Family H/o of CAD
- Lipid status (Stratified as per NCEP/ ATP III guidelines)

The patients were interviewed by the dietician of our hospital regarding their dietetic pattern using a 7 days dietary recall questionnaire. The patients were interviewed with their wives and family members regarding their usual diet in the preceding last week prior to admission to the hospital. This was analysed and daily intake of fat, carbohydrate protein and total calories of each patient was tabulated and compared with recommended dietary allowance 2010 guidelines for Indians (Report of the Expert Group of ICMR).

**Inclusion criteria**
Males and female patients from 18 to 75 years of age with proven CAD in coronary angiogram were enrolled in the study after informed consent, if they satisfied the criteria for residence in rural area as per 2011 census guidelines and National Sample Survey Organisation (NSSO)

**Exclusion criteria**
- Patients with evidence of CAD not willing for the study.
- Patients from
- Patients with CAD with renal disease with serum creatinine of more than 1.5 mg/dl.
- Cardiogenic shock/ hemodynamic instability.
- Patients with valvular heart disease.

**Sample size:** Using nMaster software at power of 80% and alpha error of 5% and as per the previous data on rural prevalence of CAD we calculated the sample size of 145.

**Sampling technique:** Non probability convenient sampling method.

**Expected outcome:** The dietary pattern and proportion of risk factors contributing to CAD will be known. By analyzing the dietary pattern and risk factors in CAD, population based prevention strategies can be devised for the rural population.

**Statistical Analyses**
All statistical analysis was performed using Statistical Package for Social Science (SPSS, version 17) for Microsoft windows. Descriptive statistics were presented as numbers and percentages. The data were expressed as Mean and SD. Independent sample student t test were used to compare continuous variables between two groups. Pearson’s Chi square test was used to evaluate whether distributions of categorical variables differed from one another a two sided p value <0.05 was considered statistically significant.

**Results**
Among the 148 patients who underwent coronary angiogram, 39.9% (59 patients) had normal coronaries, 29.1% (43 patients) had SVD, 17.6% (26 patients) had DVD and 13.5% (20 patients) had TVD. There was male preponderance of 73% in this study. Male and female were equally distributed in CAD and normal group (P = 0.24).

Height (P = 0.9), weight (P = 0.65) and BMI (P = 0.07) did not reach statistical significance between the two groups. Among the risk factors, incidence of hypertension was 29.7% (44 patients) of which 32.6% (29 patients) had evidence of CAD. Patients with hypertension tended to have CAD more often (OR: 1.4, 95% C.I: 0.6 – 2.9), however this did not reach statistical significance (P = 0.35). In diabetic subset 69.1% (38 patients) had evidence of CAD. Patients with hypertension tended to have CAD more often (OR: 1.4, 95% C.I: 0.6 – 2.9), however this did not reach statistical significance (P = 0.35). In diabetic subset 69.1% (38 patients) had evidence of CAD. The Odds ratio for DM was 1.84 (95% C.I: 0.912 – 3.717) though not statistically significant (P = 0.08), implying more incidence in patients with CAD.

The mean energy intake was 11,555 Kcal per week. The mean fat intake was 213 g per week and mean carbohydrate intake was 2087.23 g per
week. The actual energy intake between patients with CAD and normal coronaries were not statistically significant (P = 0.46) (Fig: 1). The actual carbohydrate intake was not statistically significant between the two groups (P = 0.797) (Fig: 1). The actual fat intake was not statistically significant between the two groups (P = 0.63) (Fig: 1). Protein intake was not statistically significant between the two groups (P = 0.081) (Fig: 1). Post Hoc Test analysis showed that the intake of fat or protein did not vary among patients with single, double or triple vessel disease (Fig:2) (Table 2). With increase in carbohydrate intake there was a significant increase in single vessel disease compared to normal coronaries (P = 0.03). However the mean carbohydrate intake was less in double/ triple vessel disease when compared to single vessel disease.

**Figure 1:** Comparison of intakes of energy, carbohydrate, fat and protein (mean and SD) between CAD and normal coronaries

**Figure 2:** Comparison of intakes of energy, carbohydrate, fat and protein (mean and SD) between normal, SVD, DVD and TVD.
Table 1: Comparison of baseline parameters

| S. No | Parameter          | Normal coronaries N=59 | Coronary artery disease N=89 | P value |
|-------|--------------------|-------------------------|-------------------------------|---------|
| 1.    | Sex                | Male = 67%               | 76%                           | 0.24 (NS) |
|       |                    | Female = 33%             | 24%                           |         |
| 2.    | Age                | 52.9 ± 13.4              | 55.2 ± 11.4                   | 0.26 (NS) |
| 3.    | BMI                | 23.5 ± 3.64              | 24.8 ± 4.41                   | 0.07 (NS) |
| 4.    | DM                 | 29%                     | 43%                           | 0.08 (NS) |
| 5.    | HTN                | 25%                     | 32.5%                         | 0.35 (NS) |
| 6.    | Carbohydrate (gm)  | 1979.81 ± 276.4          | 1995.74 ± 418                 | 0.79 (NS) |
| 7.    | Fat (gm)           | 211.39 ± 31.6            | 214.23 ± 37.1                 | 0.63 (NS) |
| 8.    | Protein (gm)       | 377.57 ± 51.6            | 394.07 ± 58.4                 | 0.81 (NS) |
| 9.    | Energy (Kcal)      | 11537.82 ± 1406.5        | 11542.8 ± 1662.7              | 0.9 (NS) |

Data was represented by mean ± standard deviation / percentage
NS – Not Significant

Table 2: Comparison of intakes in patients with single, double or triple vessel disease

| Dependent Variable | (A) CAG | (B) CAG | Mean Difference (A-B) | P value | 95% Confidence Interval |
|--------------------|---------|---------|-----------------------|---------|-------------------------|
|                    |         |         | Lower Bound           | Upper Bound |                      |
| ENERGY INTAKE      | NORMAL  | SVD     | -101.0554             | .988 (NS) | -917.410 – 715.299      |
|                    |         | DVD     | 160.1225              | .974 (NS) | 1132.722 – 812.477      |
|                    |         | DVD     | 151.1025              | .982 (NS) | 1206.035 – 903.830      |
|                    | SVD     | NORMAL  | 101.0554              | .988 (NS) | -715.299 – 917.410      |
|                    | DVD     | 261.1779 | .912 (NS)             | -66.413 – 1288.769 |
|                    | DVD     | 252.1579 | .934 (NS)             | -853.679 – 1357.995 |
|                    | DVD     | NORMAL  | -160.1225             | .974 (NS) | -1132.722 – 812.477    |
|                    | SVD     | -261.1779 | .912 (NS)             | -1288.769 – 766.413 |
|                    | DVD     | -9.0200  | 1.000 (NS)            | -1234.740 – 1216.700 |
|                    | DVD     | NORMAL  | -151.1025             | .982 (NS) | -1206.035 – 903.830    |
|                    | SVD     | -9.0200  | 1.000 (NS)            | -1234.740 – 1216.700 |
|                    | DVD     | 9.0200   |                      |            |                        |
| PROTEIN INTAKE     | NORMAL  | SVD     | -25.93564             | .097 (NS) | -54.0988 – 3.0375      |
|                    |         | DVD     | -6.93887              | .954 (NS) | -41.4572 – 27.5795     |
|                    |         | DVD     | -13.25167             | .794 (NS) | -50.6921 – 18.1888     |
|                    | SVD     | NORMAL  | 25.93564              | .097 (NS) | -3.0375 – 54.0988      |
|                    | DVD     | 18.99678 | .530 (NS)             | -17.4733 – 55.4669 |
|                    | DVD     | 12.68398 | .835 (NS)             | -26.5631 – 51.9311 |
|                    | DVD     | NORMAL  | 6.93887               | .954 (NS) | -27.5795 – 41.572      |
|                    | SVD     | -18.99678 | .530 (NS)             | -55.4669 – 17.4733 |
|                    | DVD     | -6.31280 | .982 (NS)             | -49.8146 – 37.1890 |
|                    | DVD     | NORMAL  | 13.25167              | .794 (NS) | -24.1888 – 50.6921     |
|                    | SVD     | -12.68398 | .835 (NS)             | -51.9311 – 26.5631 |
|                    | DVD     | 6.31280  | .982 (NS)             | -37.1890 – 49.8146 |
| FAT INTAKE         | NORMAL  | SVD     | -8.4536               | .622 (NS) | -26.625 – 9.718        |
|                    |         | DVD     | 3.8650                | .967 (NS) | -17.875 – 25.515       |
|                    |         | DVD     | 3.2111                | .985 (NS) | -20.271 – 26.693       |
|                    | SVD     | NORMAL  | 8.4536                | .622 (NS) | -9.718 – 26.625        |
|                    | DVD     | 12.3186  | .502 (NS)             | -10.555 – 35.192 |
|                    | DVD     | 11.6647  | .608 (NS)             | -12.951 – 36.280 |
|                    | DVD     | NORMAL  | -3.8650               | .967 (NS) | -25.515 – 17.785       |
### Discussion

India has witnessed a 3-fold increase in the prevalence of coronary heart disease in the last 2 to 3 decades. Coronary artery disease occurs about 10 years earlier than western countries. This has been largely due to the rapid westernisation of diet. Data from Indian surveys report that cardiovascular mortality correlated with dietary fat intake, obesity and increased sugar intake.

In western data, observational studies have noted that intake of saturated fat as a percentage of calories were strongly correlated with coronary death rates. However, meta-analysis has shown that saturated fats are not associated with all-cause mortality, CVD, CHD, ischemic stroke, or type 2 diabetes, but the evidence is heterogeneous with methodological limitations.

This could be explained by recent metabolic studies which have demonstrated that substitution of carbohydrate for saturated fat reduces total cholesterol levels (and LDL cholesterol), but also reduces HDL cholesterol and increases fasting triglyceride levels. Substitution of monounsaturated fat (or polyunsaturated fat) for saturated fat similarly reduces LDL cholesterol but does not reduce HDL or increase triglycerides. Thus, the ratio of total cholesterol to HDL cholesterol, which appears to summarize well the relation between serum lipids and CHD, is not appreciably influenced by saturated fat intake. However, when unsaturated fat replaces carbohydrate, HDL increases and LDL changes little, suggesting benefit.

Since observational studies are prone to bias related to recollection of diet history, prospective studies provide more concrete relation to diet and CHD. The Nurses’ Health study after 14 years follow up showed that saturated fat was only weakly and not significantly associated with risk of CHD, which is consistent with its lack of effect on the total cholesterol to HDL ratio. In contrast, monounsaturated fat was associated with a modestly lower risk of CHD, and polyunsaturated fat (specifically linoleic acid) was associated with a substantially lower risk. The strongest association was with intake of trans fatty acids.

Pooled analysis of prospective cohort studies has also shown that intake of saturated fat was not associated with higher risk of CHD when compared to the same percentage of energy from carbohydrates (for a 5% increase in saturated fat, RR = 0.97, 95% CI 0.81–1.16), but saturated fat was associated with higher risk if compared to polyunsaturated fat (for 5% of energy replacement, RR = 1.25, 95% CI 1.01–1.56). Total

|                  | SVD | DVD | SVD | DVD | SVD | DVD | SVD | DVD |
|------------------|-----|-----|-----|-----|-----|-----|-----|-----|
|                  | -12.3186 | -6.539 | .502 (NS) | 1.000 (NS) | -35.192 | -27.938 | 10.555 | 26.630 |
|                  | -3.2111 | .985 (NS) | -26.693 | 20.271 |
|                  | -11.6647 | .608 (NS) | -36.280 | 12.951 |
|                  | .6539 | 1.000 (NS) | -26.630 | 27.938 |
|                  | -164.08216 | .031 | -317.4335 | -10.7308 |
|                  | 80.52653 | .662 (NS) | -102.1752 | 263.2283 |
|                  | 15.03083 | .997 (NS) | -183.1370 | 213.1987 |
|                  | 164.08216 | .031 | 10.7308 | 317.4335 |
|                  | 244.60869 | .007 | 51.5768 | 437.6406 |
|                  | 179.11299 | .117 (NS) | -28.6174 | 386.8433 |
|                  | -80.52653 | .662 (NS) | -263.2283 | 102.1752 |
|                  | -244.60869 | .007 | -437.6406 | -51.5768 |
|                  | -65.49570 | .881 (NS) | -295.7460 | 164.7546 |
|                  | -15.03083 | .997 (NS) | -213.1987 | 183.1370 |
|                  | -179.11299 | .117 (NS) | -386.8433 | 28.6174 |
|                  | 65.49570 | .881 (NS) | -164.7546 | 295.7460 |

* The mean difference is significant at the 0.05 level. NS – Not Significant
fat intake was not associated with risk of CHD\textsuperscript{10}. However, the limitation is that the studies use only baseline data.

Trials involving diet modification are also difficult to interpret, since some studies the control group had changed their diet pattern. MRFIT trial and Women’s Health Initiative trial are large trials which failed to show significant difference CHD mortality\textsuperscript{11,12}. The Oslo Heart Study provided convincing relation between dietary fat intake and CHD. Dietary intervention involved primarily a reduction in saturated fat and cholesterol; polyunsaturated fat intake increased only slightly. During the intervention period, serum cholesterol fell by 17\% compared with the control group after 1 year, and after 5 years. After 5 years, the incidence of nonfatal myocardial infarction and fatal CHD was significantly (47\%) lower in the intervention group compared with controls\textsuperscript{13}.

In secondary prevention trials involving diet modification it noted that the trials involving overall fat reduction, or replacement of saturated fat by carbohydrate, had minimal effect on serum total cholesterol levels or CHD incidence. However, in trials focusing on the substitution of unsaturated for saturated fats, both serum cholesterol and CHD incidence were reduced\textsuperscript{14}.

Lyon Heart Study trial noted a significant large (70\%) reduction in recurrence of CHD was seen amongst patients with CHD assigned to the ‘Mediterranean-type diet’ compared with those on the control diet, patients with CHD were randomized to a typical low-fat diet or to a ‘Mediterranean-type diet’ that included high intake of Unsaturated fat from rapeseed oil, abundant consumption of fruits and vegetables and low intakes of red meat and dairy fat\textsuperscript{15}.

Total trans-fat intake has been found to be significantly associated with all-cause mortality (1.34, 1.16 to 1.56), CHD mortality (1.28, 1.09 to 1.50), and total CHD (5). Nurses’ Health Study has shown that the greatest benefit comes from replacement of trans fat to PUFA, more than when saturated fat is replaced by PUFA. This can be explained by diet study by Mensink et al in which 10\% of energy as trans fatty acids raised LDL-cholesterol similar to saturated fat and also reduced HDL, when both were compared to monounsaturated fat. This resulted in a significant rise in total cholesterol to HDL ratio by trans-fat compared to saturated fat\textsuperscript{16}. Total fat and saturated and unsaturated fats were not significantly associated with risk of myocardial infarction or cardiovascular disease mortality\textsuperscript{17}.

In our study, we found that overall energy intake was lower than recommended. The total fat intake was higher than that recommended for their age and body weight. The mean fat intake is not statistically significant among patients with CAD and controls (Fig: 1). Also the mean protein and carbohydrate intake was not different between CAD and controls (Fig: 1). We noted that the percentage of saturated fat intake was not different among controls and all grades of coronary artery disease (Fig: 2). The carbohydrate intake was significantly more in patients with single vessel CAD, but there was no significant difference in intake in patients with double / triple vessel CAD as compared to normal coronaries (Table 2). We noted that the percentage of saturated fat intake was not different among controls and all grades of coronary artery disease. The actual amount of trans-fat intake in our population is difficult to calculate, since the usage of foods with trans-fat was almost non-existent. However, whether repeated reheating of vegetable oils was used for frying, is not clearly studied. The usage of fruits and green leafy vegetables was also very less in our patients. This could explain the increased incidence of CHD in the Indian rural population.

A meta-analysis of effect of fruit and vegetable intake on coronary heart disease found that the risk of CHD was decreased by 4\% [RR (95\% CI): 0.96 (0.93–0.99), \textit{P} = 0.0027] for each additional portion per day of fruit and vegetable intake and by 7\% [0.93 (0.89–0.96), \textit{P} < 0.0001] for fruit intake\textsuperscript{18}. Similarly, in the INTERHEART study it was found that reduced fruit and vegetable intake is one of the important reasons for myocardial infarctions worldwide and in Indian population.
Rastogi et al., found a strong inverse relationship between intake of vegetables and ischemic heart disease\cite{19}.

Hence from this study we can conclude that the risk of Coronary artery disease in the rural population of Tamil Nadu was not related to the total carbohydrate intake, overall fat intake and percentage of saturated fat. In our study population Coronary artery disease could be related poor intake of vegetables and fruits. The role of trans-fat in the diet these patients have to be evaluated by further studies. The role of psycho-social stress which we believe is very high also needs to be evaluated.

**Limitations of the study**

It is a single centre pilot study. This result needs to be confirmed by multi-centric study involving larger cohort of patients.

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Abbreviations
ADA – American Diabetes Association
CAD – Coronary Artery Disease
CHD – Coronary Heart Disease
CI – Confidence Interval
CV – Cardio Vascular
DM – Diabetes Mellitus
DVD – Double Vessel Disease
HDL – High Density Lipoprotein
ICMR – Indian Council of Medical Research
JNC – Joint National Committee
LDL – low Density Lipoprotein
OR – Odds Ratio
NCEP / ATP III – National Cholesterol Education Program – Adult Treatment Panel
PUFA –Poly Unsaturated Fatty Acids
RR – Relative Risk
SVD – Single Vessel Disease
WHO – World Health Organisation
TVD – Triple Vessel Disease.