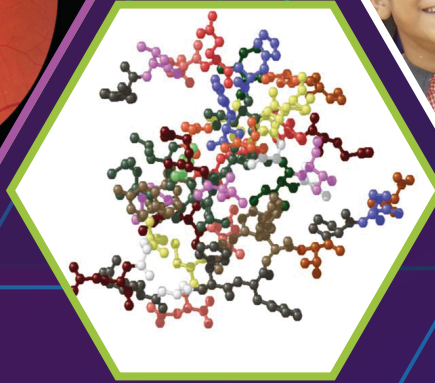
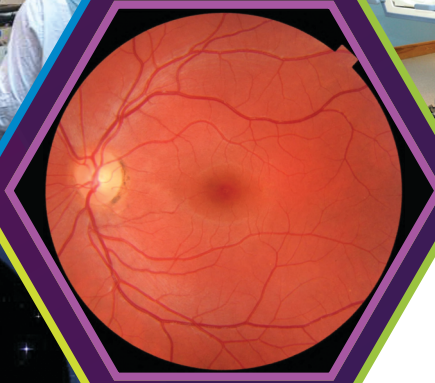
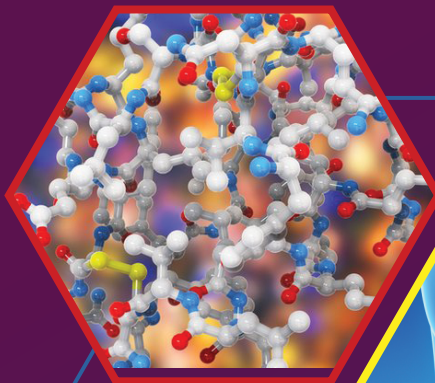


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# Association of dietary fiber intake with serum total cholesterol and low density lipoprotein cholesterol levels in Urban Asian-Indian adults with type 2 diabetes

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### ABSTRACT

**Context:** There is little data correlating dietary fibre (DF) intake and cardiovascular risk in Asian Indians with diabetes. **Aim:** To assess the DF intake and its association with lipid profile (total serum cholesterol and low density lipoprotein [LDL] - cholesterol levels) in urban Asian Indians with diabetes. **Subjects and Methods:** Dietary assessment using validated Food Frequency Questionnaire was conducted in 1191 free-living adults with known diabetes in the Chennai Urban Rural Epidemiology Study. Subjects taking medication for dyslipidemia, and those with cardiovascular disease and implausible energy intake ( $n = 262$ ) were excluded, leaving 929 participants. Anthropometric and relevant biochemical parameters were measured using standardized techniques. **Results:** Diabetic individuals who consumed DF <median intake (29 g/day) had a higher prevalence of hypercholesterolemia (49.5% vs. 40.1% [ $P = 0.01$ ]) and higher LDL cholesterol (46.2% vs. 35.5% [ $P = 0.001$ ]) than those in the > median intake of DF group. The risk of hypercholesterolemia (odds ratio [OR] = 1.38 [95% confidence interval [CI]: 1.02–1.85],  $P = 0.04$ ), and high LDL cholesterol (OR: 1.43 [95% CI: 1.06–1.94],  $P = 0.02$ ) was higher among those whose DF intake was less than the median. Serum triglycerides and high density lipoprotein cholesterol were not associated with DF intake. The main sources of DF were vegetables and legumes. **Conclusion:** In urban Asian Indians with diabetes, lower DF intake is positively related to total cholesterol and LDL cholesterol levels.

**Key words:** Asian Indians, Chennai urban rural epidemiology study, dietary fibre, low density lipoprotein, total cholesterol, type 2 diabetes

## INTRODUCTION

Diabetes is one of the leading causes of mortality worldwide, contributing directly or indirectly to more than 4.6 million deaths annually.<sup>[1]</sup> Cardiovascular disease (CVD)

is the predominant cause of mortality in individuals with diabetes.<sup>[2]</sup> CVD in diabetes is multifactorial, with abnormalities in serum lipids being one of the major risk factors. Interventions targeted at reducing low density lipoprotein (LDL) cholesterol have shown benefit in reducing the risk of CVD in individuals with diabetes.<sup>[3]</sup> One of the strategies that have been attempted for this purpose is increasing the dietary fiber (DF) intake. DF is a nondigestible carbohydrate and includes nonstarch polysaccharides, resistant oligosaccharides, resistant starch and lignin.<sup>[4]</sup> DF intake has been shown to reduce plasma lipid profile, and improve glycemic response in Caucasian population.<sup>[5-7]</sup> Unfortunately, there is little data on this topic from India, which accounts for 62.4 million individuals with

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diabetes.<sup>[8]</sup> Hence, this study was undertaken evaluate the association of DF with hyperlipidemia (total cholesterol and high LDL in particular) in urban Asian Indians with type 2 diabetes.

## SUBJECTS AND METHODS

### Subjects

This study is a sub study of the Chennai Urban Rural Epidemiology Study (CURES), which is a large epidemiological study representing the urban population of Chennai in southern India. The detailed methodology of this study has been published elsewhere.<sup>[9]</sup> Briefly, in Phase 1 of CURES, individuals aged 20 years and above were studied with 99% confidence interval (CI) and 0.5% error a sample size range of 16,000-24,000 was calculated. Further considering additional 10% dropout of diabetic subjects a total of 26,001 subjects were determined for the first phase of the study. In Phase 2 of CURES, all known diabetic subjects ( $n = 1529$ ) identified from Phase 1 were invited to the center for more detailed studies. Of these, 1191 participated in the present study (response rate, 78%). Individuals with unrealistic reported energy intake, that is, males with <800 or >4000 kcal/day and females with <500 or >3500 kcal/day ( $n = 149$ ) were excluded which included 27 people who were on lipid lowering drugs. An additional 53 subjects who were on lipid lowering drugs and those with a history of ischemic heart disease ( $n = 60$ ), were also excluded.<sup>[10]</sup> Finally, a total of 929 participants were included for the present analysis.

### Clinical and anthropometric measurements

Demographic data, medical history, drug history and data on smoking and alcohol consumption were obtained. Anthropometric measurements including height, weight and waist measurements and blood pressure measurements were obtained by trained research assistants using standardized techniques. Hypertension was diagnosed based on self-reported hypertension on drug treatment, or measured blood pressure  $\geq 135/85$  mmHg.<sup>[11]</sup>

### Biochemical assessment

Fasting plasma glucose (glucose oxidase-peroxidase method), serum cholesterol (cholesterol oxidase-peroxidase-amidopyrine method), serum triglycerides (TG) (glycerol phosphate oxidase-amidopyrine method) and high density lipoprotein (HDL) (direct method-polyethylene glycol-pretreated enzymes) were measured using a Hitachi 912 auto analyzer (Roche Diagnostics, Mannheim, Germany). LDL cholesterol level was calculated using the Friedewald formula.<sup>[12]</sup>

Diagnosis of diabetes was based on the WHO Consulting Group criteria, that is fasting plasma

glucose  $\geq 126$  mg/dl ( $\geq 7.0$  mmol/l) or 2 h postload plasma glucose (2 h PG)  $\geq 200$  mg/dl ( $\geq 11.1$  mmol/l) or self-reported diabetic subjects on treatment by a physician.<sup>[13]</sup> National Cholesterol Education Program<sup>[14]</sup> guidelines were used for definition of dyslipidemia as it is considered more appropriate for the treatment of diabetes individuals.<sup>[15]</sup> (Hypercholesterolemia: Serum cholesterol levels  $\geq 200$  mg/dl [ $\geq 5.2$  mmol/l]; hypertriglyceridemia: Serum TG levels  $\geq 150$  mg/dl [ $\geq 1.7$  mmol/l]; low HDL cholesterol: <40 mg/dl [ $<1.04$  mmol/l] in men and <50 mg/dl in women [ $<1.30$  mmol/l]; high LDL cholesterol:  $\geq 130$  mg/dl [ $\geq 2.6$  mmol/l]).

### Dietary assessment

A validated interviewer administered meal based food frequency questionnaire (FFQ) was used to measure the habitual dietary intake. Details of this FFQ have been published elsewhere.<sup>[16]</sup> Individuals were asked to estimate their usual serving size and frequency of consumption for each food item listed in the FFQ. EpiNu, an in-house database was used to assess the average daily food and nutrient intake including DF intake.

### Statistical analysis

Statistical software package SPSS (10.0 version; SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Subjects were divided based on their median intake of total DF. Normally distributed data were represented as mean and standard deviation and tested using one-way ANOVA. Values not normally distributed were represented as median and inter quartile range and tested using Mann Whitney analysis. Chi-square was used to test categorical variables. The association between total DF intake, total cholesterol and LDL cholesterol was determined using logistic regression and variables that showed significant association on univariate analysis were adjusted.  $P < 0.05$  was considered as significant.

## RESULTS

The study included 929 urban Asian-Indian adults with known diabetes from Chennai in South India. Participants were divided based on median DF consumption (29 g/day) into those with >median intake and <median intake. Details of the participants grouped based on their DF intake are shown in Table 1. Majority of female subjects consumed less than the median amount of DF ( $n = 273$  [58.8%]). In addition, those who consumed >median intake of DF had higher rates of literacy and income compared with those did not.

There were no significant differences in alcohol consumption, body mass index (BMI), waist circumference and HbA1c between the two DF groups. However, a significantly



higher proportion of subjects were found to have hypercholesterolemia (49.5%) among those consuming less than the median intake of DF ( $P = 0.01$ ). Similarly, a higher proportion of subjects (46.2%) had high LDL cholesterol levels in the <median DF group ( $P = 0.001$ ). There were no significant differences in the prevalence of generalized and central obesity, hypertension, low HDL cholesterol levels and hypertriglyceridemia between the two groups.

Tables 2 and 3 show that subjects with lower DF intake had significantly higher daily intake of carbohydrate calories (67.4 [8.4] %E) and refined cereals (330[219] g/day), dietary glycemic load (213.4 [133]) and weighted glycemic index (GI) (64.3 [3.4]) ( $P < 0.001$  for all the above). However, subjects who consumed more DF had significantly higher daily intake of protein (11.8 [1.4] %E), fat (25.5 [5.8] %E/d),

saturated fatty acids (SFA) (8.7 [2.6] %E/d), monounsaturated fatty acids (MUFA) (7.2 [1.9] %E/d), polyunsaturated fatty acids (PUFA) (8.2 [3.0] g/day), whole cereals milled (28.7 [43.5] g/day), legumes and pulses (57.7 [29.5] g/day), leafy and other vegetables (127 [81.5] g/day), fruits (33.6 [49.5] g/day), milk and its products (358.7 [245.4] g/day), visible fats and oils (33.1 [14.6] g/day) and added salt (9.0 [3.6] g/day).

Table 4 shows the logistic regression model with cholesterol as the dependent variable and DF as independent

**Table 1: General characteristics of diabetic subjects according to the median DF intake (n=929)**

Characteristics	<Median DF intake (n=464)	>Median DF intake (n=465)	P value*
Median intake of DF (g/day)	25.0	33.7	
Women n (%)#	273 (58.8)	229 (49.2)	<0.01
Age (years)‡	50.0 (16)	50.0 (14)	0.06
Smoking status: Yes n (%)#	69 (14.9)	87 (18.7)	0.12
Alcohol: Yes n (%)#	103 (22.2)	107 (23.0)	0.77
BMI (kg/m <sup>2</sup> )‡	24.5±5.6	24.7±5.2	0.33
Waist circumference (cm)‡	89.2±13.0	90.4±12.0	0.07
Literacy n (%)#	238 (80.4)	278 (87.1)	0.02
Fasting plasma glucose (mg/dl)	147 (110)	142 (88)	0.17
Postprandial plasma glucose (mg/dl)	269 (144)	263 (140)	0.62
Fasting insulin (µU/ml)	10 (9)	11 (9)	0.71
Household income/month (INR)# n (%)			
<2000	144 (50.2)	94 (30.4)	<0.001
2000-5000	119 (41.5)	169 (54.7)	
>5000-20,000	24 (8.4)	46 (14.9)	
Over weight and generalised obesity* (≥23 kg/m <sup>2</sup> ) n (%)#	310 (67.0)	322 (69.2)	0.48
Central obesity (male≥90 cm: female (≥80 cm) n (%)#	309 (70.5)	323 (71.9)	0.65
Hypertension (mmHg) n (%) (≥140 mmHg systolic BP: ≥90 mmHg diastolic BP)#	141 (30.5)	152 (32.7)	0.48
Glycosylated hemoglobin n (%) (≥7%)	327 (70.6)	336 (72.4)	0.55
Hypercholesterolemia n (%) (>200 mg/dl)#	229 (49.5)	186 (40.1)	<0.01
High LDL cholesterol n (%) (≥130 mg/dl)#	209 (46.2)	159 (35.5)	<0.01
Low HDL cholesterol n (%) (male≤40 mg/dL: female≤50 mg/dl)#	318 (68.5)	334 (72.0)	0.25
Hypertriglyceridemia n (%) (>150 mg/dl)#	221 (47.7)	228 (49.1)	0.67

‡Data are represented as median interquartile range (IQR) in parentheses (all such values) and Mann-Whitney test for such variables, \*Categorical value represented in proportion and tested by Chi-square, \*P<0.05 considered significant. BMI: Body mass index, BP: Blood pressure, HDL: High density lipoprotein, LDL: Low density lipoprotein, DF: Dietary fiber

**Table 2: Dietary intake of the diabetic subjects according to the median DF intake (n=929)**

Dietary factors	<Median DF intake (n=464)	>Median DF intake (n=465)	P value
Total energy intake (kcal/day)‡	2143 (1116)	2238 (814)	0.08
Total protein % E‡	11.1 (1.7)	11.8 (1.4)	<0.001
Total carbohydrates % E‡	67.4 (8.4)	62.8 (6.4)	<0.001
Glycemic load‡	213.4 (132.9)	181.7 (79.5)	<0.001
Weighted GI‡	64.3 (3.4)	60.9 (3.6)	<0.001
Total fat % E‡	21.1 (6.6)	25.5 (5.8)	<0.001
Total DF (15-25 g/1000 kcal) n (%)‡	459 (98.9)	157 (33.8)	<0.001
Total SFA % E‡	7.9 (3.0)	8.7 (2.6)	<0.001
Total MUFA % E‡	6.3 (2.1)	7.2 (1.9)	<0.001
Total PUFA % E‡	5.7 (3.1)	8.2 (3.0)	<0.001
Total trans fatty acid % E‡	0.03 (0.05)	0.03 (0.05)	0.12

‡Data are represented as median IQR in parentheses (all such values) and Mann-Whitney test for such variables, \*Categorical value represented in proportion and tested by Chi-square, \*P<0.05 considered significant. GI: Glycemic index, DF: Dietary fibre, IQR: Interquartile range. PUFA: Polyunsaturated fatty acid, MUFA: Monounsaturated fatty acid, SFA: Saturated fatty acid

**Table 3: Intake of food groups according to median of energy adjusted DF intake of the representative population of 929 urban subjects with diabetes**

Food groups (g/day)	<Median DF intake (n=464)	>Median DF intake (n=465)	P value
Cereal-refined‡	330 (218.6)	256.3 (138.4)	<0.001
Cereal-whole milled‡	10.3 (16.4)	28.7 (43.5)	<0.001
Milletts (g/day)‡	0 (0.13)	0 (0.75)	0.002
Legumes and pulses‡	39.0 (21.4)	57.7 (29.5)	<0.001
Tubers (g/day)‡	5.5 (13.3)	5.6 (10.4)	0.97
Other vegetables‡,§	81 (57)	127 (81.5)	<0.001
Fruits (g/day)‡	22.4 (43.5)	33.6 (49.5)	<0.001
Milk and milk products‡,***	300.3 (277.1)	358.7 (245.4)	0.03
Egg (g/day)‡	9.7 (11.2)	12.3 (12.0)	0.86
Meat and poultry‡	10.6 (16.3)	10.6 (10.6)	0.50
Fish and seafood‡	15.3 (15.9)	13.1 (16.9)	0.04
Fats and oils‡	22.9 (13.8)	33.1 (14.6)	<0.001
Nuts and oilseeds‡	14.6 (9.5)	19.5 (11.1)	<0.001
Added sugar‡	6.4 (14.1)	5.1 (9.0)	<0.001
Added salt‡	6.6 (4.2)	9.0 (3.6)	<0.001

‡Data are represented as median IQR in parentheses (all such values) and Mann-Whitney test for such variables, \*Categorical value represented in proportion and tested by Chi-square, \*P<0.05 considered significant other vegetables include leafy vegetables; other vegetables and roots, \*\*\*Dairy products include milk, yoghurt and buttermilk. IQR: Interquartile range, DF: Dietary fiber

variable. The subjects with DF intake below the median had a higher risk of having hypercholesterolemia (odds ratio [OR] = 1.38; 95% CI: 1.02–1.85;  $P = 0.03$ ) and high LDL cholesterol (OR = 1.43; 95% CI: 1.06–1.94;  $P = 0.02$ ) even after adjusting for confounding variables such as age, sex, smoking, duration of diabetes, BMI, blood pressure, TG, carbohydrates, fats, and total added sugar.

Figure 1 shows the quality of DF food sources in both groups. In both the groups, the main sources of DF were vegetables (10.4 g/day vs. 6.3 g/day) followed by legumes (7.2 g/day vs. 4.7 g/day). The DF contribution from refined cereals was higher in those consuming below the median intake (3 g/day) of DF intake compared with those above (2.5 g/day).

**Table 4: OR and 95% CI of dyslipidemia in subjects with type 2 diabetes according to median of DF intake**

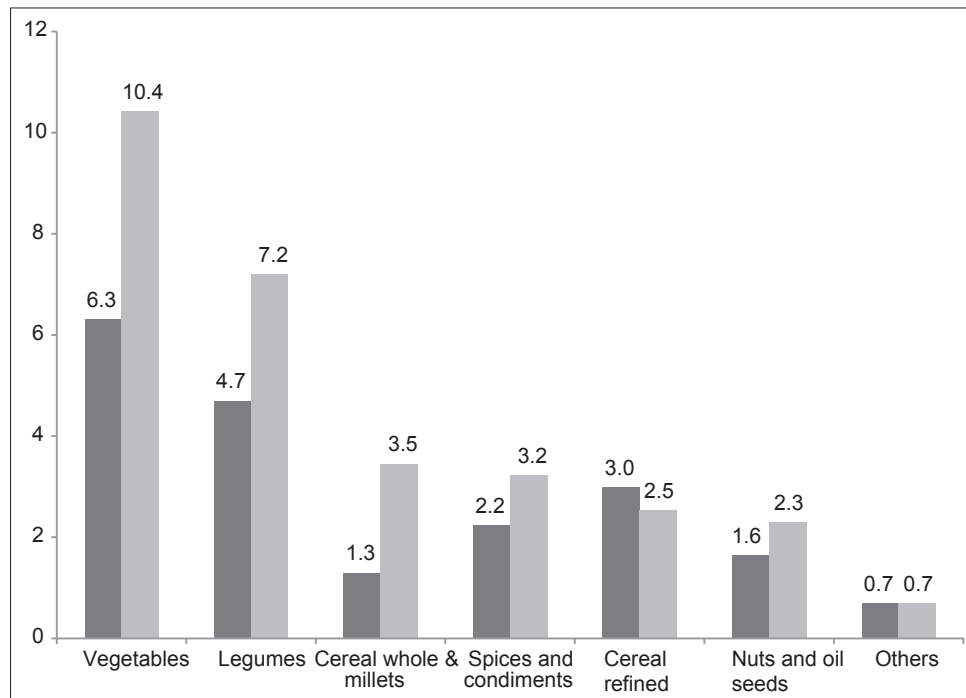
Variables	>median DF intake (reference)	<median DF intake (odds and 95% CI)	P value
Hypercholesterolemia	1	1.38 (1.02-1.85)	0.03
High LDL cholesterol	1	1.43 (1.06-1.94)	0.02
Low HDL cholesterol	1	0.77 (0.55-1.06)	0.11
High TG	1	0.89 (0.66-1.19)	0.43

Variables are adjusted for age (years), sex (male, female), smoking (yes/no), diabetes duration (years), BMI ( $\text{kg}/\text{m}^2$ ), BP (mmHg), TG (mg/dl), total PUFA (g/day), total MUFA (g/day), total SFA (g/day), total added sugar (g/day). OR: Odds ratio, CI: Confidence interval, HDL: High density lipoprotein, LDL: Low density lipoprotein, DF: Dietary fiber, BMI: Body mass index, BP: Blood pressure, TG: Triglyceride, PUFA: Polyunsaturated fatty acid, MUFA: Monounsaturated fatty acid, SFA: Saturated fatty acid

## DISCUSSION

The present study reveals an inverse association of total DF intake with total cholesterol and LDL cholesterol levels among urban adults with type 2 diabetes. Individuals who consumed less than the median DF intake (<29 g/day) had 38% and 43% higher risks for hypercholesterolemia and high LDL cholesterol compared with those consuming more than the median intake of DF. Our results are consistent with the findings of earlier studies carried out in western populations.<sup>[5,17,18]</sup>

A randomized crossover study trial on individuals with type 2 diabetes in the United States showed a decrease of 6.7% in total cholesterol and 12.5% in very LDL levels with a high-fiber diet.<sup>[17]</sup> Our study showed 4% lower total cholesterol and 6% lower LDL cholesterol in high DF intake group compared to low DF intake group. Similarly, a low GI diet having high DF (34 g/day) showed a significant decrease in total serum cholesterol and LDL cholesterol and no significant reduction was observed in the low DF diet (20 g/day) in type 2 diabetic men.<sup>[18]</sup> Other studies carried out in healthy individuals have also shown an inverse association between DF intake and LDL cholesterol. A 45 days supplementation trial of high fiber diet on healthy Indians of various incomes groups showed a significant reduction in LDL cholesterol by 3% in low income, 8% in middle income and 10% in high income group but showed no change in HDL levels.<sup>[19]</sup>



**Figure 1:** Dietary fiber (DF) (g/day) contribution of different food groups in the diets of subjects with type 2 diabetes all food groups are significant at  $P = 0.001$  <median DF intake >median DF intake

Several possible mechanisms by which fiber lowers blood cholesterol have been suggested by earlier studies. The physicochemical properties of DF alter metabolic pathways of hepatic cholesterol and lipoprotein metabolism, resulting in lowering of plasma LDL-cholesterol.<sup>[20]</sup> The fiber binds with bile acids or cholesterol during the formation of micelles (viscous gel like structure), which results in reduction of cholesterol content of hepatic cells. This results to up-regulation of the LDL receptors and further increases clearance of LDL cholesterol from the blood circulation.<sup>[5,21]</sup> This gel formation also slows gastric emptying, maintains satiety and helps in reducing weight.<sup>[22]</sup> Other suggested mechanisms include inhibition of hepatic fatty acid synthesis by products of fermentation of the soluble fibers such as short chain fatty acids and resistant starch in small intestine which help to reduce the plasma lipid levels.<sup>[23]</sup>

The mean intake of DF in our study ( $29.0 \pm 7.4$  g/day) was higher than those reported elsewhere in the world. In the European diabetic population, mean intake of DF was reported to be  $23.4 \pm 4.8$  g/day<sup>[24]</sup> and in US diabetic population from the National Health and Nutrition Examination Study, the mean DF intake was 16.9 (11.3-25.4) g/day in men and 11.6 (7.9-16.6) g/day in women.<sup>[25]</sup> The Strong Heart Study (1997-1999) reported DF intake of 15.1 (9.2-23.3) g/day in men and 13.4 (8.8-19.6) g/day in women with known diabetes.<sup>[26]</sup> In the present study, the DF intake reported by diabetic men was  $30 \pm 8.6$  g/day and women  $28.8 \pm 6.2$  g/day. Although our study subjects reported higher DF intake compared to western population, it did not meet the national recommended intake (40 g/2000 calories).<sup>[27]</sup> Almost 90% of the study population in the present study consumed less than the recommended levels indeed. In addition American Dental Association also recommends to choose a variety of fibre containing foods such as legumes, whole grain products (fibre-rich cereals  $\geq 5$  g fibre/serving), fruits and vegetables in the diet to manage diabetes.<sup>[28]</sup>

In our study, the group with more intake of DF had higher consumption of good sources of DF such as legumes, vegetables, whole cereals, nuts and oil seeds. However, they also consumed more milk and milk products and visible fat and oil which are rich sources of SFA, MUFA and PUFA [Table 3]. The nature of fatty acids consumed independently plays a major role in altering lipid profile particularly total cholesterol and LDL.<sup>[29]</sup> These parameters were adjusted in the regression model as confounding variables to show the independent association of DF intake and LDL cholesterol.

The higher DF group of this study derived most of their DF from vegetables (10.4 g/day) and legumes (7.2 g/day) and the whole grains consumption was meager (3.5 g/day) [Figure 1].

The present study also indicates that subjects with high consumption of DF from vegetables and legumes have lower prevalence of hypercholesterolemia. Our earlier study among nondiabetic individuals in Chennai showed a 5% lower in total serum cholesterol and 8% lower LDL cholesterol levels in the individuals who were in the highest quartile of fruits and vegetables intake and they also had 48% lower risk of CVD.<sup>[30]</sup> In the same population, intake of refined grains (white rice) was also shown to be positively associated with metabolic syndrome and type 2 diabetes.<sup>[31,32]</sup>

Our study shows that DF intake is dependent on income levels, possibly due to higher cost of foods rich in DF. It appears to be difficult for individuals in the lower income group to find inexpensive foods with higher levels of DF.<sup>[19,33]</sup> Recent reports have also showed there was nearly a threefold difference in legume and vegetable consumption between high and low income groups in India.<sup>[34,35]</sup> The National Family Health Survey 3 (2005-06) survey also recorded that weekly consumption of fruit increases from 16% in the low income group to 72% in the high income group.<sup>[36]</sup>

The relation of DF intake with HDL is not consistent. Clinical trials in healthy adults have shown that higher intake of DF did not show any association with TG and HDL cholesterol.<sup>[37,38]</sup> However, a meta-analysis by Brown *et al.*<sup>[5]</sup> showed that HDL cholesterol levels are significantly reduced in few trials with no difference in TG levels with increased intake of soluble fiber. Our findings show a small decrease in HDL levels (though not significant) amongst those who consumed more DF. The mechanism behind the reduction of HDL levels is unknown and need to be explored in future studies.

In our study population, there was no significant difference in the mean HbA1c levels between those who consumed more than the median DF and those who consumed less than the median. Chandalia *et al.* have shown that a very high intake of DF ( $>50$  g/day) is required to produce improvements in glycemic control (HbA1c) in the diabetic population.<sup>[17]</sup> The absence of significant differences in HbA1c between the groups in our study might perhaps have been because only 1% of subjects consumed such a high quantity of DF.

This is, to our knowledge, one of the first studies to evaluate the relationship between DF intake and CVD risk factors in an Asian Indian diabetic population. One of the strengths of our study is the validated FFQ, which has shown high reproducibility and validity for total carbohydrates, GI, glycemic load and DF. One of the limitations of the study is that it is a cross-sectional one, which does not allow for inferences on cause and effect. The second limitation is

that the study has not identified the type of DF consumed due to lack of information on insoluble and soluble fiber content for many Indian foods.

## CONCLUSION

The present study reports an inverse association between DF intake and hypercholesterolemia and high LDL cholesterol levels in subjects with type 2 diabetes in urban Chennai. Policy level changes are needed to ensure better accessibility and affordability of fiber rich foods such as fruits, vegetables, legumes and whole cereals to promote DF intake along with healthier cooking methods to reduce the CVD burden in the diabetic population.<sup>[31]</sup>

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