Diet and Diabetes in Relation to Coronary Artery Disease*

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ABSTRACT

The prevalence rate of diabetes in Indians appears to be greater than that of Western populations . This may be due to rapid changes in diet and lifestyle of urbans resulting in central obesity. Beta-cells of pancreas and arterial endothelial cells are highly susceptible to damage due to free radicals and diet deficient in antioxidant vitamins A,E and C. Carotene may not be able to provide necessary protection resulting in a decrease in insulin action and development of diabetes mellitus. Insulin resistance becomes worst in presence of higher dietary fat intake leading to central obesity and associated disturbances. It seems that antioxidant deficiency and central obesity are two independent risk factors of non-insulin dependent diabetes which also predisposes to CVD. The prevalence rates of diabetes mellitus (8.6%) and of CAD (8.6%) in our study were comparable with industrialised countries. For each, quintile of waisthip ratio (WHR) above 0.88, dietary fat intake was higher and physical activity lower than that for lower WHR. Plasma insulin, blood glucose and triglycerides for each upper quintile of WHR were significantly higher than for lower quintiles. It is possible that populations with higher prevalence of diabetes and cardiovascular risk can be benefitted by increased intake of antioxidant rich foods such as fruits, vegetables and oils. It seems that any increase in fat intake beyond 21% energy per day, any increase in body mass index above 21 and WHR beyond 0.88 should be avoided to prevent diabetes and CVD. "Eating at least 600g/day of fruits, vegetables and legumes especially before major meals can decrease cardiovascular risk" is the major conclusion of our research.

INTRODUCTION

The interactions between diet, diabetes, human health, the surrounding environment and the responses of the body are so variable that we can accept no single universal theory regarding development of diabetes and its complications. Diabetes is a polygenic disease and therefore multiple mechanisms are likely to be involved in the pathogenesis of its complications. There is evidence that in the pathogenesis of macrovascular disease in diabetes (NIDDM), endothelial damage is the basic event which results in atherosclerosis and thrombosis. Of the three important pathways for development of macrovascular disease, hyperlipidaemia is related to dietary fat, insulin resistance to central obesity and free radical stress to lower intake of antioxidant vitamins E,C and beta-carotene. There is a rapid emergence of diabetes, hypertension, stroke and coronary artery disease (CAD) in the urban populations of most developing countries with rapid changes in diet and lifestyle [1, 2]. Reliable population-based data on death rates due to diabetes and other chronic diseases are not available from India. However, a few small studies [3] from India and several population-based studies among South Asian immigrants to industrialised countries show that prevalence rate of diabetes and CAD in Indians are comparable or greater than that in the industrialised countries [4]. In South Asian immigrants to UK, higher prevalence of diabetes and CAD [5] have been associated with central obesity, glucose intolerance, hyperinsulinaemia, hypertension, hypertriglyceridaemia and lower high density lipoprotein-cholesterol. In Europeans [6], central obesity is a strong predictor of CAD than weight for height. It seems that majority of the risk factors of diabetes are related to diet and lifestyle factors among them. Dietary fatty acids, antioxidant vitamins, soluble fibre and sedentary habits, all may be important in the pathogenesis of increased risk of diabetes, its complications and mortality [1, 2, 8]. We do not agree with Mckeigue and associates that diet is not important in the development of diabetes and CAD in Indian immigrants to UK [5].

Free Radical Stress

Beta cells of pancreas and vascular endothelium are highly susceptible to oxygen derived free radicals and diet deficient in antioxidant vitamins A,E and C. Betacarotene may not be able to provide the necessary protection against oxidants present in the environment [9]. Omega-6 fatty acids (that are abundant in cell membranes) found in simple sugars are a major source of oxygen free radicals from the diet. Free radicals are produced by various bioch2mical reactions in physiological and pathological states which utilise oxidase or oxygenase enzymes. Beta cells of pancreas and vascular endothelial cells appear to

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have lowest potential for scavenging these reactive elements. Recently, in a few case control studies, plasma levels of antioxidant vitamins E and C were inversely related to diabetes and its vascular complications in association with increased lipid peroxides [8, 10]. In one study, which comprises of a random sample of 152 urbans [8], plasma levels of vitamin C and carotene were lowered and lipid peroxides higher in patients with diabetes and glucose intolerance than in subjects without any risk factors. Smokers also showed a similar deficiency which suggests that smoking may have adverse effects on diabetes and its complications (Table 1).

Table 1
Plasma levels of antioxidant vitamins and lipid peroxides in diabetes mellitus and subjects without risk factors in the Peerzada Prospective Study. Values are mean (Standard deviation) [8].

µmol/l	Smokers (n=36)	Diabetes mellitus (n=13)	Glucose intole-rance (n=12)	No risk factors (n=92)
Vitamin C	22.5(3.1)**	20.2(2.8)**	25.4(3.4)*	42.5(4.5)
Vitamin E	19.6(2.9)	15.6(2.7)*	17.2(2.1)*	21.4(3.2)
Vitamin E/ choleslerol ratio	3.82(0.58)	2.88(0.48)*	3.2(0.50)*	4.2(0.56)
Vitamin A	2.01(0.22)	2.1(0.23)	2.3(0.26)	2.4(0.25)
Beta-carotene	0.32(0.06)**	0.31(0.05)**	0.41(0.06)*	0.55(0.08)
Lipid peroxides (nmollml)	2.95(0.25)**	2.86(0.22)**	2.23(0.20)	1.6(0.20)

P value obtained by analysis of variance by comparison of smokers and diabetes with no risk factors group. = P<0.01, '=P<0.001.

Dietary consumption of vitamin C and beta-carotene were significantly lowered in smokers and diabetics than in subjects without any risk factors (Table 2).

Table 2
Vitamin intake in smokers and diabetes patients in relation to subjects without risk factors [1].

Vitamins	Smokers (n = 36)	Diabetes mellitus (n=13)	Glucose intole-rance (n=12)	No risk factors (n=92)
Vitamin C (mg/1000 Kcal/day)	27.8(3.3)**	30.5(3.2)**	38.6(3.8)	37.5(3.8)
Vitamin E (mg/1000 Kcal/day)	4.1 (0.5)	4.2(0.4)	4.1(0.4)	4.6(0.6)
Vitamin A (µg/1000Kcal/day)	223(17)	225(14)	230(16)	228(19)
Beta-carotene (µg/1000Kcal/day)	629(28)*	624(30)*	640(32)	693(38)

p value obtained by analysis of variance = P<0.05, ' = P<0.01.

There is some evidence that smokers avoid eating fruits and vegetables as a habit due to loss of taste. Similarly, diabetics may have avoided eating fruits because of their sweet taste for fear of increasing blood glucose which appears to be more likely because in glucose intolerance, the intake of vitamins was normal. Lower plasma levels in patients with glucose intolerance indicate that antioxidants are utilised to quench the free radicals produced during defective metabolism. It is possible to conclude that in populations with higher prevalence of diabetes, antioxidant deficiency increases the risk and they may be benefitted by increased consumption of fruits, vegetables and legumes (vitamins A,C, carotene), seeds and oils (vitamins E). Plasma levels of antioxidants have not been reported in Indian immigrants to industrialised countries. Since fruits and vegetables are expensive in UK, it is possible that there is a relative decrease in the consumption of these foods in immigrants, although it may be still greater than in Britons.

The prevalence of diabetes in Indian immigrants to UK was 20% which is 2.5 times higher than in Indian urbans. The prevalence rate of diabetes in our study was little higher than in Britons (8.6 vs 5.0%). Body weight, body mass index and waist-hip ratio (WHR) as well as sedentariness, fasting and post-prandial plasma insulin levels were comparable with Britons and do not explain the cause of higher prevalence of diabetes (8.6%) and CAD (8.6%) in the Indian urbans. Dietary fat and refined carbohydrate intake were higher and fruit and vegetable intake were comparable in Britons compared to Indians which indicate that dietary factors do not appear to be the cause of higher prevalence of diabetes in Indians [8], Similarly, total cholesterol level was lower than Britons showing that serum cholesterol is not the cause of higher CAD in Indians. The exact mechanism of free radical stress in diabetes is not known. There may be increased non-enzymatic glycosylation and auto-oxidative glycosylation as well as metabolic stress resulting from changes in the level of inflammatory mediators and the status of antioxidant defense systems and localised tissue damage resulting from hypoxia and ischaemic reperfusion injury. It appears that there is a critical balance between free radical generation and antioxidant defenses [9]. The extent of tissue damage may be the result of free radicals generated and the balance with available antioxidant defense system. Cell membrane lipids are vital for the maintenance of cellular integrity and survival. Peroxidation of membrane lipids [11] can result in the inactivation of enzymes and cross-linking of membrane lipids and proteins and cell death. It seems that hyperglycaemia and hyperinsulinaemia

can damage the endothelial cell membrane in different target organs due to membrane lipid peroxidation resulting into angiopathy which becomes greater in presence of hyperlipidaemia. The adverse effects of oxidative stress in diabetes appear to be independent of the adverse effects caused by lipids in the pathogenesis of angiopathy leading to atherosclerosis and thrombosis resulting in CAD, hypertension, stroke, nephropathy and retinopathy [9,10].

Is there a need for further analysis of data?

Further analysis of data in the same epidemiologic study are necessary to find out other possibilities because diet and lifestyle factors and their beneficial or adverse effects vary from one community to the other community [2, 12, 13]. Mckeigue, Sah and Marmot [5] have done a similar mistake by comparing Indian immigrants to UK with Britons. These authors reported that dietary fat, plasma cholesterol, BMI and physical activity status do not explain the cause of 4 times higher prevalence of diabetes and 40% higher death rate due to CAD in Indian immigrants than in Britons. The authors neither studied antioxidants nor they tried to compare Indian immigrants with Indian urban and rural populations while making the above conclusions. It is difficult to say whether they ignored the low fat intake and low prevalence of CAD in Indian rural population just to publish their views in Lancet [5].

In our study [8], there were 80 males and 72 females and the prevalence rate of central obesity was 53.9% (n=82) which is higher than the prevalence of generalised obesity (25.0%) reported in urbans in the Delhi study [12]. The prevalence of central obesity was significantly higher among sedentary (52.4%, $p<0.01$) subjects and mild activity group (30.5%, $p < 0.05$) compared to moderate and heavy activity group. The criteria of central obesity was WHR above 0.88.

We took 0.88 as a dividing line as against 0.85 by Mckeigue and associates because our median WHR was 0.88 and in another Indian study [13, 14], WHR>0.88 was taken as abnormal. The prevalence of diabetes mellitus and glucose intolerance according to quintiles of WHR was significantly higher in each of upper quintile of WHR above 0.88 than in the lower quintiles. However, the BMI were comparable in each quintiles (Table 3). Similarly, energy expenditure during routine physical activity were lower and dietary fat intake higher in each of the upper quintiles of WHR than in the lower quintiles (Table 4). Similar findings are expected if diet and physical activity data are re-analysed in the study among Indian immigrants to Britain (5).

Table 3

Waist-hip girth ratio in quintiles and prevalence of diabetes and glucose intolerance in relation to physical activity and dietary fat consumption.

	Waist-hip girth ratio				
	> 0.92	**0.89-0.92**	**0.85-0.88**	**0.81-0.84**	**< 0.81**
Number of subjects	20	31	31	31	39
Glucose intolerance (%). Mean (SD)	7(35.0)*	4(12.9)*	1(3.2)	–	–
Diabetes mellitus (%), Mean (SD)	4(20.0)*	7(22.5)**	1(3.2)	1 (3.2)	–
Body mass index (kg/m^2). Mean (SD)	23.2(4.0)	22.6(3.7)	22.0(3.2)	22.1(3.1)	20.6(3.0)
Energy expenditure (Kcal/day). Mean (SD)	1026(96)*	1082(91)*	1505(116)	1485(105)	1410(116)
Dietary fat intake (% Kcal/day), Mean (SD)	31.0(2.1)**	28.3(1.8)**	23.6(1.5)	21.5(1.4)	19.2(1.2)

P value obtained by comparison of higher quintiles above 0.88 with lower quintile of WHR between 0.85-0.88.
* =P<0.05, ** =P<0.01.

Table 4

Plasma insulin and blood glucose levels in relation to Waist-hip girth ratio

	Waist-hip girth ratio				
	> 0.92	**0.89-0.92**	**0.85-0.88**	**0.81-0.84**	**<0.81**
Number of subjects	20	31	31	31	39
Fasting blood glucose, mg/dl (SD)	112.5(12.2)**	108.2(8.9)**	103.0(7.5)**	90.1 (7.0)**	86.2(6.6)
Post-prandial blood glucose, mg/dl (SD)	155.3(13.1)**	153.4(11.5)**	144.5(9.6)**	136.6(10.6)*	132.5(9.5)
Fasting plasma insulin, mu/l (SD)	11.6(3.9)**	9.5(3.1)**	6.4(2.6)**	4.1(1.7)**	3.0(0.6)
Post-prandial plasma insulin, mu/l (SD)	32.5(5.6)**	28.3(4.8)**	22.0(3.7)**	15.5(2.8)**	12.2(2.4)

P values were obtained by comparison of each of higher quintiles of WHR above 0.88 with~WHR 0.85-0.88 and of lower quintiles group with lowest WHR group. * = P<0.05, ** = P<0.01.

Insulin resistance, central obesity and fat intake

The subjects in our study had a modest tendency for central obesity, glucose intolerance and associated disturbances with higher prevalence of diabetes (8.6%) and CAD (8.6%). Fasting and post-prandial plasma insulin, blood glucose and triglyceride levels were significantly higher in each of the upper quintiles of WHR in a graded manner with increase in WHR. Total cholesterol were comparable and blood pressures were higher in the upper quintiles but significantly lower in the lowest quintile of WHR. However, the BMI was comparable (Table 4). Post-prandial plasma insulin levels were much greater among Indian immigrants indicating definite insulin resistance [5].

The occurrence of obesity reflects the interaction of dietary fat and physical activity with inherited predisposition (2). Glucose intolerance and insulin resistance are associated with a pattern of obesity in which high proportion of body fat is deposited on the trunk and in the abdomen which is characteristic of obesity in South Asians [5]. In developed countries, a BMI of 20-25 with an average value of 22 is taken as normal indicating that majority of the population in developed countries is obese because their BMI ranges from 24-26 [2, 6]. In Indian immigrants to UK, dietary fat intake is 38% of the energy intake per day, body mass index is 25-26 and the WHR is 0.98 in males and 0.86 in females. In Britain, the fat intake is 40-45% of energy from fat, body mass index 24-26 but the WHR is only 0.94 in males and 0.76 in females.

In developing countries [2], the lower limit of normal BMI may be 18.5 and an average BMI of 20 may be considered appropriate. Since an average BMI above 23 is usually associated with CAD, this level may be considered upper limit of normal. There is increasing evidence that central obesity presents a greater hazard which is much greater in South Asians than Europeans [5, 7]. A WHR of more than 0.85 is considered at higher risk [5]. However, it appears to be too low for South Asians because of their short stature and a tendency for central obesity and moreover a majority of our urban population with little or no risk of chronic diseases would be included at risk. Therefore, in Indians, as suggested in the present study, a WHR above 0.88 should be considered as central obesity and BMI should be least considered. WHR increases when energy intake is in excess of expenditure for a sustained period of time. Since dietary fat is particularly conducive to weight gain [2], it may be a major cause of central obesity in South Asians and in Indian immigrants to Britain.

Diet

Epidemiologic studies show that as the total fat content of the diet increases, an increasing proportion of persons within the population develop obesity and associated chronic diseases [2]. Intersalt study in adults showed that a mean BMI of 22-23 is associated with a dietary fat content that provides 15-20% energy [2]. In Brazil, with mean BMI of 22, the fat content of diet amounts to 18% of energy intake [2]. In Europeans [2, 6], a mean BMI of 25-26 is associated with a dietary fat intake of 35-40% of energy from fat sources. In our study, a mean BMI of 22 and a WHR between 0.81-0.88 was associated with an intake of 21-23% energy from fat. There is no evidence of the association of WHR with fat intake. According to our study, any increase in fat intake beyond 23.6% energy is likely to be associated with diabetes and cardiovascular disease in conjunction with central obesity. On grounds of central obesity alone, any increase beyond 21% energy from fat (7% each saturated, polyunsaturated and monounsaturated fatty acids), any increase in BMI beyond 21 and any increase in WHR beyond 0.88 should be avoided. Rest of the calories may be from proteins (14%) and carbohydrates (65%). While saturated fatty acids can predispose to hyperlipidaemia, thrombosis and diabetes, polyunsaturated fatty acids especially of n-6 variety can cause increased lipid peroxidation and increased oxygen derived free radical generation which are important in the pathogenesis of diabetes. atherosclerosis and thrombosis [9, 11]. These complications can be prevented by increased consumption of antioxidant nutrients, soluble dietary fibre and n-3 fatty acids [10]. It should be noted that majority of Indian urbans are eating the step 1 diet of the American Heart Association, therefore this diet is unlikely to provide protection against CVD to Indians as well as to other population eating lower amount of fat and cholesterol.

World Health Organisation Study Group [2] advises the intake of at least 400g/day of fruits and vegetables for prevention of chronic diseases. These foods if taken before the meals also decrease the intake of fat and refined carbohydrates as well as provide fibre, flavin, flavonoids, antioxidant vitamins and minerals. There is now sufficient evidence that majority of the complex carbohydrates should be supplied through increased consumption of fruits. vegetables and legumes especially in diabetes because these foods protect against hyperglycaemia and hyperlipidaemia as well as free radical stress in diabetes [9, 13]. In one study [13], we reported that eating 400g/day of guava fruit was associated with significant decline in blood lipids, blood pressures,

blood glucose and oxidative stress with rise in plasma level of vitamin C. It seems that diet is very important in the development of central obesity, diabetes and CVD in Indians.

In conclusion, it may be emphasised that prevention of diabetes in developing countries, particularly in South Asians, is little different than in the developed countries. Target levels of risk factors for body weight, BMI, WHR and dietary fat intake are lower, whereas the limits for physical activity, fruit, vegetable and n-3 fatty acid intake may be higher than in the developed countries. Such strategies have been found to decrease the coronary risk in patients with risk factors of CAD.

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