Online Journal of Health and Allied Sciences
Peer Reviewed, Open Access, Free Online Journal
Published Quarterly : Mangalore, South India : ISSN 0972-5997
Volume 9, Issue 3; Jul-Sep 2010

Original Article:

Cardiovascular Risk Factors in Normolipidemic Acute Myocardial Infarct Patients on Admission – Do Dietary Fruits and Vegetables Offer Any Benefits?

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Citation: Kumar A, Sivakanesan R. Cardiovascular Risk Factors in Normolipidemic Acute Myocardial Infarct Patients on Admission – Do Dietary Fruits and Vegetables Offer Any Benefits? *Online J Health Allied Scs.* 2010;9(3):3
URL: http://www.ojhas.org/issue35/2010-3-3.htm
Open Access Archives: http://cogprints.org/view/subjects/OJHAS.html and http://openmed.nic.in/view/subjects/ojhas.html

Submitted: Aug 9, 2010; Accepted: Sep 28, 2010; Published: Oct 15, 2010

Abstract:
Background: Myocardial Infarction (MI) is a leading cause of death in India. Whether dietary vitamins could reduce risk of cardiovascular disease among Indians is still not clear and very few studies have addressed the association between dietary vitamin acting as an antioxidant or pro-oxidant and its effect on risk reduction or aggravation in normolipidemic AMI patients. **Objective:** The goal of the current study was to address the association between dietary vitamin and cardiovascular risk in normolipidemic acute myocardial infarct patients compared with healthy controls. **Design:** Dietary intake of vitamins was assessed by 131 food frequency questionnaire items in both AMI patients and age/sex-matched controls. The associated changes in risk factors due to antioxidant vitamins intake was also assessed in normolipidemic acute myocardial patients and was compared with controls. **Results:** Dietary intake of vitamin A, B1, B2, B3 was significantly higher in AMI patients compared to healthy controls but the intake of vitamin C was significantly higher in controls compared to AMI patients. Even though the vitamins intake was higher in patients, the associated cardiovascular risk factors were not reduced compared to controls. The total cholesterol, LDL-c, TAG were significantly higher ($p<0.001$) in AMI patients except HDL-c which was significantly higher ($p<0.001$) in controls. The endogenous antioxidants were found to be significantly lowered in patients compared to controls in spite of higher vitamin intake. Similarly the enzymatic antioxidants were also significantly lowered in patients. The mean serum Lipoprotein (a) malondialdehyde (MDA) and conjugated diene (CD) levels in patients were significantly elevated compared with controls. The levels of caeruloplasmin, C-reactive protein, fibrinogen, ischemia-modified albumin were significantly higher but arylesterase activities were lowered in patients. **Conclusion:** Diets rich in vegetables and fruits do not seem to reduce the cardiovascular risk in normolipidemic AMI patients among Indians and Sri Lankans.

Key Words: Dietary vitamins; Acute myocardial infarction; Cardiovascular risk factors; Normolipidemia; India; Sri Lanka

Introduction:

Cardiovascular disease (CVD) is a major cause of morbidity and mortality in the Western World. In recent years, its steep rise has alarmed common man and raised its importance internationally among scientists and researchers, and it is going to be the major cause of mortality in the globe by 2020.[1] It is a multifactorial disease associated with factors like heredity, hyperlipidemia, obesity, hypertension, environmental and life style variables like stress, smoking, alcohol consumption, etc.[2]

The World Health Organization predicts that deaths due to CVD are projected to double between 1985 and 2015.[3,4] Asian Indians living abroad have a 40% higher risk of ischemic heart disease (IHD) mortality than that for Europeans.[5] Researchers across the world are emphasizing their researches to prevent or minimize this increase in the death rate due to CVD. When it comes to prevention and regression of this disease, dietary management comes as the first line of management and emphasis is placed on a dietary regimen rich in antioxidants.[6] It is believed that oxidative stress is involved in the pathogenesis of atherosclerosis; while a variety of antioxidants have been used in clinical trials and studies during the past few years, a very clear cut message is still awaited from the studies.[7] American Heart Association has taken long standing commitment to provide information related to nutritional role in risk reduction of future episodes of CVD.[8] No clear cut dietary regimen in antioxidant vitamins have still been provided for prevention of this disease; even though vitamins act as antioxidants, at times can also act as pro-oxidants and nullify the antioxidant effect of other antioxidants if consumed in the form of cocktail.[9] In the present study, the dietary antioxidant vitamins were assessed in AMI patients and were compared with healthy controls. The study also aimed to observe the variation in risk factors in patients and controls due to variation in diet-

ary vitamins intake which was estimated using three 24-hour dietary records from the food stuffs which are generally consumed among Indians and Sri Lankans. The study also measured anthropometric details among the two groups along with risk factors which could be associated in causation of myocardial infarction.

Materials and Methods:

Cases: Eligible cases were all patients aged 48-69 y hospitalized with a diagnosis of first incident acute myocardial infarction (MI) in Sharda Hospital, Greater Noida, India and Peradeniya Hospital, Faculty of Medicine, Peradeniya, Sri Lanka from 12 September 2004 to 16 February 2007. The definitive diagnosis of AMI was established according to diagnostic criteria: chest pain lasting for ≤3 hours, electrocardiographic (ECG) changes (ST elevation ≥ 2 mm in at least two leads) and elevation in enzymatic activities of serum creatine phosphokinase and aspartate aminotransferase. The control group consisted of 165 age/sex-matched healthy volunteers (123 men and 42 women).

Inclusion criteria were patients diagnosed of AMI with normal lipid profile. Patients were excluded if they had any previous history of MI or IHD (including bypass surgery, angina, or stroke) because such prior diagnoses may alter behaviors, including diet. Patients with diabetes mellitus, renal insufficiency, hepatic disease or taking lipid lowering drugs or antioxidant vitamin supplements were also excluded from the study. We also excluded patients if they were pregnant, had a history of cancer, gastrointestinal tract infection, or thyroid, because these conditions may have affected dietary intake. The patients were interviewed on average 2–5 d after admission. The eligibility criteria were met by 245 cases, and 165 were included in the study. The reasons for exclusion were death (n = 19) or discharge (n = 27) before the interviews could be completed, being too sick to be interviewed (n = 16), and not giving consent to participate (n = 18).

Controls: For each case subject, 2 control subjects matched by age (within 5 y), sex, and hospital were obtained from noncardiac outpatient clinics or inpatient wards. The same exclusion criteria used for cases were applied for control selection as well. We identified ≈ 165 eligible control subjects. Controls were selected by using predominantly any of these two methods depending on the hospital. In the first method, we accompanied a particular physician during an outpatient clinic, according to a weekly schedule of clinics and wards. At the end of each consultation, the physician or the physician's assistant invited the patient to speak with us about his or her lifestyle and diet. Patients matching the required age and sex profile were eligible according to study criteria and were then informed of the study and asked to participate. In these situations, participation was 100%. In the second method, we independently identified control patients from clinics and wards. We attempted to approach all individuals present during a particular outpatient clinic or in a specified ward. In large clinics, patients were screened for eligibility and invited to participate according to their queue number (highest number first). This method was used to prevent bias in the selection of controls. Overall participation was high, ≈ 98%. Basic demographic information was collected from all persons who were approached. If an individual fit the required age and sex profile and was eligible, we briefly explained the study and asked whether the person was willing to participate.

Criteria for Normolipidemics: Normal lipid profile was defined if LDL was <130mg/dL, HDL ≥ 35 mg/dL, Total cholesterol (TC) <200 mg/dL and Triglycerides (TG) <150 mg/dL.[10]

Data Collection: Interviews were conducted in the hospital wards or clinics by us and lasted ≈ 30 min. Informed consent was obtained from all study subjects. This included various life style factors such as education, socio-economic status, income and type of job. Details of major cardiovascular risk factors such as smoking, alcohol intake, diabetes, obesity and hypertension were also obtained. We also collected data on socioeconomic status; smoking history; history of hypertension, diabetes, and hypercholesterolemia; family history of cardiovascular disease (including IHD, angina, MI, hypertension, diabetes, stroke, sudden death, and bypass surgery); dietary intake; types of fat or oils used in cooking; nutritional supplement use; and physical activity.

Dietary intake by 24-hour dietary record:[11] The patients and controls were given the food items which they were supposed to mark including the quantity consumed. This was carried for three times in the same subjects to avoid bias and to get more accuracy. The dietary intake was tabulated and the amount of vitamins was calculated from the food consumed.

Anthropometric measurements: Anthropometric measures (height, weight, and hip and waist circumferences) were obtained and body mass index (weight in kg divided by height in meters squared) and waist-to-hip ratio were calculated. Their blood pressures were recorded. Height was measured in centimeters and weight in kilograms using calibrated spring balance. Supine waist girth was measured at the level of umbilicus with a person breathing silently and standing hip girth was measured at inter-trochanteric level. Waist and hip measures were assessed by using a standardized tape measure, with waist measures taken at the midpoint between the costal margin and ileac crest and hip measures taken at the widest circumference.

Blood Pressure: The blood pressure was measured using standard mercury manometer. At least two readings at 5 minutes intervals as per World Health Organization guidelines were recorded.[12] If high blood pressure (≥140/90 mmHg) was noted, a third reading was taken after 30 minutes. The lowest of the three readings was taken as blood pressure.

Electrocardiogram: Electrocardiogram (12 lead) was performed on all persons using proper standardization.

Collection of Samples: Blood (10 ml) was collected after overnight fasting in different containers.

EDTA vial: 5.0 ml of blood was taken. Red cells were washed 3-4 times with ice-cold normal saline and used for estimation of glutathione peroxidase, superoxide dismutase and catalase.

Plain vial: Remaining blood was allowed to clot and serum separated by centrifugation for 5 min at 5000 rpm and was used for determination of lipid profile, malondialdehye and conjugated dienes, and other assays as described.

For IscMA analysis, 2 ml of blood was collected from the patients immediately after admission to intensive care unit.

Lipid profile: Total cholesterol, triglycerides, and HDL-cholesterol were estimated by enzymatic methods using the kits obtained from Randox Laboratories Limited, Crumlin, UK. Plasma LDL-cholesterol was determined from the values of total cholesterol and HDL-cholesterol using the following formulae:

LDL-C = TC - (TG/5) – HDL-C (mg/dl)

All chemicals of analytical grade were obtained from Sigma chemicals, India.

Serum Albumin: Serum Albumin was measured by Bromocresol green dye binding method.[13]

Serum Uric acid: Serum uric acid was estimated by the method of Brown based on the development of a blue color due to tungsten blue as phosphotungstic acid is reduced by uric acid in alkaline medium.[14]

Serum total bilirubin: Serum total bilirubin was estimated by Jendrassik and Grof method.[15]

Glutathione peroxidase: The glutathione peroxidase activity was determined by the procedure of Paglia and Valentine.[16]

Superoxide dismutase (SOD): Superoxide dismuatse enzyme activity was measured by SOD assay kit using rate of inhibition of 2-(4-indophenyl)-(4-Nitrophenol)-5-phenyltetrazolium chloride (I.N.T) reduction method modified by Sun et al.[17]

Catalase: Catalase activity was measured spectrophotometrically as described by Beutler.[18,19]

MDA: MDA levels were estimated by thiobarbituric acid (TBA) reaction.[20]

Conjugated dienes (CD): CD levels were measured by Recknagel and Glende method[21] with little modification.

Serum Ceruoplasmin: The ceruloplasmin assay was done by *p*-phenylene diamine method.[22]

All chemicals of analytical grade were obtained from Sigma Chemicals, India.

Ischemia Modified Albumin (IscMA): IscMA concentration was determined by addition of a known amount of cobalt (II) to a serum sample and measurement of the unbound cobalt (II) by the intensity of colored complex formed after reacting with dithiothreitol (DTT) by colorimeter.[23,24]

Lipoprotein (a), Lp(a): The Lp(a) levels were determined by Latex- Enhanced Turbidimetric method.

Aryesterase/Paraoxonase assay: Serum Arylesterase/Paraoxonase was estimated using Zeptometrix Assay Kit obtained from Zeptometrix Corp, New York, 14202 based on the cleavage of phenyl acetate resulting in phenol formation. The rate of formation of phenol is measured by monitoring the increase in absorbance at 270 nm at 25°C.

Ascorbic acid: Estimation of Vitamin C was carried out by Roe and Kuether method.[25]

Measurement of High sensitive C- Reactive protein (hs-CRP): The hsCRP ELISA is based on the principle of a solid phase enzyme-linked immunosorbent assay.

Plasma fibrinogen: TEClot Fib Kit 10 (TECO GmbH, Dieselstr. 1, 84088 Neufahrn NB Germany) was used for the estimation of fibrinogen.

Results:

Dietary vitamins intake was higher in AMI patients excepting for ascorbic acid which was higher in controls as shown in Table 1. Anthropometric variables in acute myocardial infarction (AMI) patients showed highly significant differences in weight, BMI, waist circumference, hip circumference, waist-hip ratio, mid-arm circumference, biceps and triceps skin fold thickness as shown in Table 2. The total cholesterol, LDL-c, TG were significantly higher ($p<0.001$) in AMI patients except HDL-c which was significantly higher ($p<0.001$) in controls as shown in Table 3. The cardiac markers enzymes are shown in Table 4. The serum endogenous antioxidants were significantly decreased in patients compared to controls. Similarly the enzyme antioxidants were also significantly lowered in patients. The mean serum Lipoprotein (a) malondialdehyde (MDA) and conjugated diene (CD) levels in MI patients were higher compared with controls as shown in Tables 5 and 6. Serum fibrinogen, ceruloplasmin, ischemia-modified albumin and C-reactive protein were significantly elevated whereas arylesterase activities were significantly lowered in cases compared with controls as shown in Table 7.

Table 1: Mean dietary intakes of vitamins in Control and AMI Patients

	Control (n=165)	AMI Patients (n=165)	P value (95%CI)
Vitamin A (µg)	2102.3 ± 425.2	2638.6 ± 154.3	<0.01(2611.33-2665.87)
Vitamin B1 (mg)	1.8 ± 0.3	2.2 ± 0.3	<0.05 (2.15-2.24)
Vitamin B2 (mg)	1.7 ± 0.2	1.9 ± 0.3	<0.001(1.85-1.94)
Vitamin B3 (mg)	19.0 ± 3.6	25.3 ± 3.6	<0.001 (24.79-24.80)
Vitamin C (mg)	460.8 ± 85.3	304.0 ± 101.5	<0.001(289.67-318.32)

Table 2: Anthropometric data of control and AMI patients (mean ± SD)

	Control (n=165)	AMI patients (n=165)	P- value (95%CI)
Age Range (years)	60.5 ± 3.4 *(48-69)*	61.8 ± 3.8 *(48-69)*	0.0037 (61.26- 62.33)
Height (m)	1.63 ± 0.04	1.64 ± 0.59	0.2919 (1.55-1.72)
Weight (kg)	68.34 ± 3.97	72.01 ± 5.37	<0.01 (71.25-72.76)
BMI (kg/m^2)	25.40 ± 1.20	26.16 ± 1.45	<0.01 (25.95-26.36)
Waist Circumference (cm)	93.70 ± 3.63	100.77 ± 6.06	<0.01 (99.91-101.62)
Hip Circumference (cm)	100.01 ± 3.16	105.72 ± 5.23	<0.01 (104.82-106.45)
Waist-Hip ratio	0.93 ± 0.01	0.95 ± 0.01	<0.001 (0.94-0.95)
Mid Arm Circumference (cm)	29.70 ± 1.47	30.63 ± 1.87	<0.01 (30.36-30.89)
Biceps skin fold thickness (mm)	6.95 ± 1.05	7.5 ± 1.38	<0.001 (7.30-7.69)
Triceps skin fold thickness (mm)	11.97 ± 1.27	12.89 ± 1.69	<0.001 (12.65-13.12)
Systolic blood pressure (mmHg)	121.06 ± 4.19	134.32 ± 11.65	<0.05 (132.67-135.96)
Diastolic blood pressure (mmHg)	79.90 ± 3.64	86.04 ± 4.25	<0.05 (85.44-86.63)

Table 3: Lipid profile in AMI patients and healthy controls (mean ± SD)

Variables	Controls (n=165)	AMI patients (n=165)	P-value (95%CI)
Age	60.55 ± 3.98	61.84 ± 3.80	0.0037(61.26-62.42)
Total Cholesterol†	168.58 ± 12.16	186.44 ± 13.95	<0.001(184.31-188.56)
HDL-Cholesterol†	50.51 ± 6.78	41.27 ± 4.62	<0.001(40.56-41.97)
Triglycerides†	107.84 ± 11.51	128.96 ± 12.19	<0.001(127.10-130.82)
LDL-Cholesterol†	83.59 ± 11.95	119.37 ± 14.05	<0.001(17.22-21.51)

* ratio † (mg %)

Table 4: Cardiac Enzyme Markers in Control subjects and AMI patients (Mean ± SD)			
	Control (n=68)	**AMI patients (n=97)**	**P value (95%CI)**
Troponin I (ng/ml)	0.23 ± 0.11	1.56 ± 1.03	<0.0001(1.41-1.70)
Troponin T (ng/ml)	0.04 ± 0.03	0.64 ± 0.42	<0.0001(0.58-0.69)
Myoglobin (ng/ml)	20.64 ± 6.37	180.87 ± 120.31	<0.0001(163.89-197.87)
CK-Total (IU/L)	0.97 ± 0.53	314.78 ± 221.13	<0.0001(283.57-345.98)
CK-MB (IU/L)	0.13 ± 0.07	67.11 ± 54.64	<0.0001(59.39-74.82)

Table 5: Antioxidant status in Control subjects and AMI patients (Mean ± SD)			
	Control *(n=165)*	**AMI patients *(n=165)***	**P value (95%CI)**
Serum albumin (mg/dl)	4.4 ± 0.3	4.2 ± 0.3	<0.0001(4.15-4.24)
Serum uric acid (mg/dl)	5.8 ± 1.2	4.3 ± 0.9	<0.0001(4.17-4.42)
Serum ascorbic acid (mg/dl)	5.3 ± 1.2	2.8 ± 0.7	<0.0001(2.70-2.89)
Serum Total bilirubin (mg/dl)	0.8 ± 0.2	0.7 ± 0.2	<0.0001(0.67-0.72)
Serum superoxide dismutase (U/gHb)	1826.5 ± 31.9	813.9 ± 208.9	<0.0001(784.42-843.37)
Serum glutathione peroxidase (U/gHb)	61.3 ± 3.9	42.6 ± 6.3	<0.0001(41.71- 43.48)
Serum catalase (k/gHb)	256.2 ± 26.7	193.1 ± 35.9	<0.0001(188.03-198.16)

Table 6: Lp(a) and Lipid Peroxidation levels in Control subjects and AMI patients (Mean ± SD)			
	Control *(n=165)*	**AMI patients *(n=165)***	**P value (95%CI)**
Serum Lipoprotein (a) (mg/dl)	3.0 ± 1.1	10.9 ± 2.2	<0.0001 (10.58-11.21)
Serum malondialdehyde (nmol/L)	5.7 ± 1.0	14.8 ± 1.7	<0.0001(14.56-15.03)
Serum conjugated dienes (µmol/L)	31.0 ± 2.7	48.3 ± 5.5	<0.0001(47.52-49.07)

Table 7: Other Biochemical parameters in Control subjects and AMI patients (Mean ± SD)			
	Control *(n=165)*	**MI patients *(n=165)***	***P* value (95% CI)**
Plasma fibrinogen (mg/dl)	237.5 ± 17.4	357.8 ± 23.2	<0.0001 (354.52 -361.07
Serum caeruloplasmin (mg/dl)	20.4 ± 2.3	51.5 ± 2.4	<0.0001 (51.16-51.83)
Serum Arylesterase activity (kU/L)	98.4 ± 6.2	69.7 ± 10.0	<0.0001(68.28-71.11)
Serum Ischemia modified albumin (U/ml)	81.9 ± 3.9	97.5 ± 11.7	<0.001(95.84-99.15)
Serum C-reactive protein (mg/dl)	1.1 ± 0.3	3.0 ± 1.1	<0.0001(2.84-3.15)

Discussion:

Coronary artery disease (CAD) remains the major cause of morbidity and mortality in all developed and developing countries in the world including India.[26] Various risk factors have been identified among which dyslipidemia is one of the major modifiable risk factors.[27-29]

The coronary artery disease risk factors do not predict the occurrence of acute myocardial infarction (AMI) as variation in risk factors is observed in South Asian population due to varied dietary habits and life style.[30] The search for various conventional risk factors among Asians could be helpful as there are always some missing links between cardiovascular disease (CVD) and risk factors associated with them. This prompted us to identify the newer risk factors and to observe the variations in known risk factors such as variation in antioxidant vitamins intake, with respect to Indian and Sri Lankan population.

Even though antioxidants and vitamins are efficient in cardioprotection and delay the progression of CVD, the search for the newer risk factors continues and now investigations are on the line to exploit the role of inflammatory markers and other potential risk factors which could link with acute myocardial infarction (AMI).

In this prospective case-control study, only normolipidaemic acute myocardial infarction (AMI) patients were selected. The study was designed to identify and evaluate potential risk factors in normolipidaemic acute myocardial infarction (AMI) patients with respect to their antioxidants intake. The subjects selected for the study comprised of 165 controls, 48-69 y and 165 acute MI patients, 48-69 y.

Antioxidants intake

The current study observed higher antioxidant vitamins consumption in patients compared to controls, excepting for vitamin C which was higher in controls. It is therefore debatable why the antioxidant status was comparatively lower in patients and risk factors observed were higher in them compared to controls, even though they had higher exogenous intake of antioxidants through the food. The basis could be partially explained with the nullifying effect of these vitamins by various inter-plays of oxidants and pro-oxidants which could have been higher in patients, that failed to provide adequate protection from oxidants.[31] Earlier studies have emphasized to increase the antioxidants in diet and clinical trials have shown effective results. Though a beneficial role for vitamins in CVD has long been explored but the data are still inconsistent and it is not affirmative with several findings. Studies show that intake of fruits and vegetables do not prevent but can instead cause metabolic syndrome and type II diabetes, which are considered as a major risk factor in cardiovascular diseases.[32] The beneficial effects of antioxidants, though supported by observational studies and randomized controlled clinical trials, have not yet supported their role in the prevention of CVD and some studies have rather indicated higher mortality in those with late-stage atherosclerosis.[33]

Studies have suggested that a combination therapy is superior over single supplementation but ongoing trials are yet to confirm.[34] Further studies have indicated that beta-carotene neutralizes the beneficial effects mediated by other vitamins as it acts as a pro-oxidant when given in supplementation cocktail. The trials that used a combination of vitamins that include beta-carotene have been disappointing.[35] However, ascorbic acid along with vitamin E in combination have shown some good results as long term anti-atherogenic effects but their combined effect on clinical endpoints has been inconsistent.[36]

Research data suggest that vitamins would be beneficial to individuals who are deficient of antioxidants or exposed to increased levels of oxidative stress such as in smokers, diabetics and elderly patients. Through defining the right population group and the optimal vitamin combination we could potentially find a future role for vitamins in CVD.

Anthropometric variables:

Anthropometric variables in acute myocardial infarction (AMI) patients showed highly significant differences in waist/hip ratio and biceps skin fold thickness. It has been reported[37] that waist / hip ratio is a dominant, independent and predictive variable of cardiovascular disease and coronary heart disease deaths in Australian men and women. Megnien et al[38] also reported high hip circumference relative to weight and waist circumference as a better predictor of low incidence of cardiovascular disease and coronary heart disease. The present study is in good agreement with the observations of the above studies. Among Indians, the cardiovascular risk is high even if the prevalence of obesity is minimal.[38] In the present study, the mean body mass index and waist / hip ratio in all subjects was 26.56 and 0.96 respectively, showing a significantly higher body mass index and weight / hip ratio in patients compared with controls.

Based on the observations of the aforementioned studies and further supported by the present study, it could be concluded that weight/hip ratio is a better predictor of cardiovascular disease (CVD) than body mass index. So it is a better, non-invasive, tool for identifying the future risk of acute myocardial infarction.

Observations on lipid profile

The mean total cholesterol level of the controls compared with acute myocardial infarction patients (186.44 ± 13.95 mg/dL) was significantly ($p<0.001$) higher compared with controls (168.58 ± 12.16 mg/dL). The mean high density lipoprotein-cholesterol level in the patients was significantly lower ($p<0.001$) compared with controls. Triglyceride (TG) values observed in AMI patients was (129mg/dL) significantly higher than controls (107.8mg/dL). The mean low density lipoprotein-cholesterol (LDL-c) levels in patients was (119.4mg/dL), significantly higher than controls (83.6 mg/dL). The total cholesterol / high density lipoprotein – cholesterol ratio in acute myocardial infarct patients (4.6) was significantly ($p<0.001$) higher compared with controls (3.4). The present study observed significantly higher ratio (2.9) in acute myocardial infarction patients compared with controls (1.9).

Earlier studies on lipid profile analysis conducted in acute myocardial infarction patients[39-50] observed higher total cholesterol, triglyceride, low-density lipoprotein–cholesterol and lower levels of high-density lipoprotein-cholesterol in patients compared to controls.

Also higher ratio of total cholesterol to high density lipoprotein-cholesterol, low-density lipoprotein-cholesterol to high-density cholesterol-lipoprotein and higher triglyceride to high-density cholesterol-lipoprotein were observed in the present study. The present study concludes the importance of assessing the lipid ratios even in normolipidemic subjects as it is one of the atherogenic factors for development of myocardial infarction and other coronary complications. The practice of computing the ratio should be implemented even in a normal health check up packages. In the final analysis it appears that myocardial infarction and coronary artery disease are not always associated with an elevated serum total cholesterol concentration. The major concern of this observation is that subjects who maintain desirable total cholesterol concentration also are targets for myocardial infarction and coronary artery disease and therefore analysis of other risk factors that are non-conventional and newly emerging will be of immense important in the eventual assessment of the risk status. The existing literature and the results of the present study all point out that acute myocardial infarction and coronary artery disease patients have significantly higher total cholesterol concentration whether the values are in the desirable range or elevated.

Antioxidant status

The serum endogenous antioxidants were decreased in acute myocardial infarction compared to controls. Similarly the enzyme antioxidants were also significantly lowered in patients.

Studies conducted[51,52] in acute myocardial infarction patients reported significantly lower ($p<0.0001$) albumin and bilirubin ($p<0.0001$), whereas lower levels of uric acid[48-50] and ascorbic acid[40,56-59] have also been reported in acute myocardial infarct patients.

The aforementioned studies suggest that the expected risk of acute myocardial infarction is increased where these endogenous antioxidants are lowered due to enhanced utilization during oxidative stress in patients. Though uric acid is a well established antioxidant, at times it can also act as a pro-oxidant, which might increase the risk of myocardial infarction. Aulinskas et al,[60] established the role of ascorbic acid as up-regulator of low density–lipoprotein (LDL) receptors, facilitating the clearance of low density–lipoprotein (LDL). The low levels of ascorbic acid in acute myocardial infarction patients in the present study might be due to enhanced utilization of ascorbic acid during oxidative stress in patients.

The enzymatic antioxidants, namely superoxide dismutase, catalase and glutathione peroxidase, are also lowered in patients compared with controls. The findings of the present study concurs with earlier studies[40,48,57,61-64] that reported lower activities of superoxide dismutase, catalase and glutathione peroxidase. Other studies[42,49,61,63-65] also reported reduced activities of glutathione peroxidase in patients compared with controls. These studies are based on the hypothesis of decreased antioxidants due to oxidative insult in myocardial infarct patients. Thus it is indicative that low levels of both endogenous and enzyme antioxidants in circulation may be due to its increased utilization to scavenge toxic lipid peroxides.

Lipoprotein (a) and lipid peroxidation:

The mean serum Lipoprotein (a) malondialdehyde (MDA) and conjugated diene (CD) levels in MI patients were higher compared with controls. Earlier studies conducted[44,63,66,67] also observed higher Lipoprotein (a) in AMI patients where as Nascetti et al,[68] did not observe any change in Lipoprotein (a) levels in cardiovascular disease patients and concluded that lipoprotein (a) should not be considered as an independent risk factor in CVD patients.

Other studies[40,42,49,57,58,61,64] have also reported higher levels of malondialdehyde (MDA) in myocardial infarct patients, as in our study.

Other biochemical parameters

The levels of ceruloplasmin, C-reactive protein, fibrinogen, ischemia-modified albumin were higher and arylesterase activities were lowered in patients. Other studies[65,69-71] also observed significantly higher ($p<0.001$) levels of ceruloplasmin and higher levels of C-reactive protein[47,72-75] in patients. Shukla et al,[76] reported elevated levels of ceruloplasmin as a risk factor for acute myocardial infarction. The reactive oxygen species disrupts copper binding to ceruloplasmin, thus impairing its antioxidant property and further promoting oxidative pathology. Other studies conducted on plasma fibrinogen levels in acute myocardial infarct patients[23,24,47,77-79] also reported rise in plasma fibrinogen as in the present study. Studies on arylesterase activities in acute myocardial infarct patients[80-86] also observed lower activities, concurring with the current study. Increased C-reactive protein (CRP) concentrations in patients with unstable angina and acute myocardial infarction might induce the production by the monocytes of the tissue

factor which initiates the coagulation process. C-reactive protein, together with fibrinogen, acts as a chemotactic factor. Fibrinogen is responsible for the adhesion of macrophages to the endothelial surface for their migration into the intima. The elevated c-reactive protein levels have been found to be related to the occurrence of cardiovascular complications such as sudden cardiac death or AMI.[87]

Conclusions:

Our study has concluded that dietary vitamins do not decrease the risk of acute myocardial infarction. There might be a number of additional risk factors interplaying in acute myocardial infarction patients, which have not been adequately protected against by the higher vitamin intake.

Limitations of the Study:

The sample size is not adequate to draw definitive conclusion. Future studies should be carried out with large scale patients sample size.

Conflicts of Interest

The authors do not have any conflict of interests from the study.

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