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Cardiovascular Risk Factors in Elderly Normolipidaemic Acute Myocardial Infarct Patients

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1. Introduction

Cardiovascular diseases (CVD) are a group of disorders of the heart and blood vessels, and include coronary heart disease (CHD), cerebrovascular disease (stroke), raised blood pressure (hypertension), peripheral artery disease, rheumatic heart disease, congenital heart disease and heart failure. According to the World Health Organization, CVD are the number one cause of death globally and claim 17 million lives each year. By 2030, almost 24 million people will die from CVD, mainly from heart disease and stroke. These are projected to remain the single leading causes of death (World Health Organization. Cardiovascular diseases (CVDs). Available from: http://www.who.int/mediacentre/factsheets/fs317/en/index.html). In the United States, CVD account for more than one-third (34.3%) of deaths annually, and responsible for nearly 3 million Americans reporting disability. The costs of CVD are also staggering. In 2010, the total cost including health care services, medications and lost productivity, is estimated to be over $503 billion in the United States (Centers for Disease Control and Prevention. Heart Disease and Stroke Prevention. Addressing the nation's leading killers: at a glance 2010. Available from: http://www.cdc.gov/chronicdisease/resources/publications/AAG/dhdsp.htm). Similarly, the National Heart Foundation of Australia reported that CVD are the leading cause of mortality and morbidity in Australia, killing one person nearly every 10 minutes (National Heart Foundation of Australia. Data and statistics. Available from: http://www.heartfoundation.org.au/information-for-professionals/data-and-statistics). Despite improvements over the last few decades, CVD remain as the second largest disease burden to our society after cancers. As the population ages, the economic impact of CVD on the health care system will become even greater. Tobacco smoking, an unhealthy diet, physical inactivity and high alcohol consumption increase the risk of CVD. Indeed, behavioral and dietary risk factors are responsible for about 80% of coronary heart disease and cerebrovascular disease (World Health Organization. Cardiovascular diseases (CVDs). Available from: http://www.who.int/mediacentre/factsheets/fs317/en/index.html).

Interestingly, both the incidence and mortality rate of CVD are much lower in Japan than other countries (Mozaffarian D) which may be attributed to the high consumption of

fish/seafood by the Japanese population (Meyer BJ). The fact that fish is abundant in omega-3 polyunsaturated fatty acids has opened an effective venue to the prevention and treatment of this disease by either dietary modifications or pharmacological supplementation.

Cardiovascular disease is multi-factorial which is associated with factors like hereditary, hyperlipidemia, obesity, hypertension, environmental and life style variables like stress, smoking, alcohol consumption, etc (Chopra and Wasir 1998). Lipoprotein profile has been investigated extensively in recent years, which is deranged in large proportion of coronary artery disease (CAD) patients; especially Asians showing a mixed picture of dyslipidemia (Vasisht *et al*, 1990). Literature survey reveals dyslipidaemic subjects are more prone to myocardial infarction, due to increased free radical generation and ischemia as it is a conventional risk factor. (Malhotra *et al*, 2003; Mishra *et al*, 2005; Ghosh *et al*, 2006; Patil *et al*, 2007; Rajasekhar *et al*, 2004; Rani *et al*, 2005; Gomez *et al*,1996). Lowering of high density lipoprotein- cholesterol (HDL-C) is a common phenomenon observed in MI patients supported by previous studies (Malhotra *et al*, 2003; Mishra *et al*, 2005; Ghosh *et al*, 2006; Patil *et al*, 2007; Rajasekhar *et al*, 2004; Rani *et al*, 2005). High density lipoprotein- cholesterol (HDL-c) is the most important independent protective factor for arteriosclerosis which underlies coronary heart disease (CHD). High density lipoprotein- cholesterol (HDL-c) associated paraoxonase-1 (PON1) enzyme is protective against lipid peroxidation (Singh *et al*, 2007). Numerous cohort studies and clinical trials have confirmed the association between a low high density lipoprotein- cholesterol (HDL-c) and increased risk of coronary heart disease (CHD). Low density lipoprotein-cholesterol (LDL-C) is considered as the most important risk factor of coronary artery disease (CAD). Its oxidized form promotes foam cells formation which initiates the process of atherosclerosis by accumulating in sub-endothelium cells leading to fatty streaks and complex fibro fatty or atheromatous plaques formation (Berliner *et al*, 1995). The oxidation of low-density lipoprotein (LDL) can be limited by antioxidant enzyme system, including superoxide dismutase, catalase, glutathione peroxidase and antioxidant vitamins C, A, E and other carotenoids. Among the endogenous antioxidant system, includes albumin, uric acid, and total bilirubin. Imbalance of this reaction either due to excess free radical formation or insufficient removal by antioxidants leads to oxidative stress (Frei *et al*, 1998; Shrinivas *et al*, 2000; Maritim *et al*, 2003).

Various other risk factors have been identified apart from dyslipidemia are caeruloplasmin, C-reactive proteins, Lipoprotein (a), plasma fibrinogen, etc. Since we have encountered myocardial infarct patients with normal serum lipid concentration, we conducted a prospective case-control study to evaluate the concentration of antioxidant enzymes, degree of lipid peroxidation and other risk factors associated with acute myocardial infarction.

2. Materials and methods

The prospective case-control study consisted of 165 patients (123 men and 42 women) with AMI, admitted to the Intensive Cardiac Care Unit (ICCU), Sharda Hospital, India. The 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 (CPK) and aspartate aminotransferase (AST). The control group consisted of 165 age/sex-matched healthy volunteers (123 men and 42 women). The design of this study was pre-approved by the

institutional ethical committee board and informed consent was obtained from the patients and controls. Inclusion criteria were patients with a diagnosis of acute myocardial infarction (AMI) with normal lipid profile. Patients with diabetes mellitus, renal insufficiency, current and past smokers, hepatic disease or taking lipid lowering drugs or antioxidant vitamin supplements were excluded from the study. Normolipidemic status was judged by the following criteria: LDL≤160 mg/dl; HDL, ≥35 mg/dl; total cholesterol (TC), <200 mg/dl; and triglycerides (TG), <150 mg/dl (NCEP, ATP-III, 2001). Ten milliliters of blood was collected after overnight fasting for lipid profile assay. For ischemia-modified albumin (IscMA) analysis, 2 ml of blood was collected from the patients immediately after admission to intensive care unit.

Lipid Profile Total cholesterol (TC), triglyceride (TG) and high density lipoprotein-cholesterol (HDL-c) were analyzed enzymatically using kit obtained from Randox Laboratories Limited, Crumlin, UK. Plasma low density lipoprotein -cholesterol was determined from the values of total cholesterol and high density lipoprotein-cholesterol using the following formula:

$$\text{LDL-cholesterol}=\text{TC} - \frac{\text{TG}}{5} - \text{HDL-cholesterol}\left(\text{mg/dl}\right)$$

Other assays - Serum albumin was measured by Bromocresol green binding method (Perry *et al*, 1979). 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 (Brown ,1945). Serum total bilirubin was estimated by the method of Jendrassik and Grof (Jendrassik and Grof, 1938).

The glutathione peroxidase (GPx) activity was determined by the procedure of Paglia and Valentine (Paglia and Valentine,1967). Superoxide dismutase (SOD) 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 (Sun *et al*, 1988). Catalase activity was measured spectrophotometrically as described by Beutler (Beutler, 1984). MDA levels were estimated by thiobarbituric acid (TBA) reaction (Bernheim *et al*, 1948).Conjugated diene (CD) levels were measured by Recknagel and Glende method (Recknagel and Glende, 1984) with little modification. Caeruloplasmin assay was done by *p*-phenylene diamine method (Ravin, 1961). Ischemia-modified albumin (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 (Libby ,2003). Lipoprotein (a), levels were determined by Latex- Enhanced turbidimetric method. Serum 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.

Estimation of ascorbic acid was carried out by Roe and Kuether method (Roe and Kuether, 1943). The C-reactive protein were determined using high sensitivity enzyme Immunoassay kit manufactured by Life Diagnostics,inc., Catalog Number: 2210. The principle of the assay was based on a solid phase enzyme-linked immunosorbent assay (Kumar and Sivakanesan,

2008). The plasma fibrinogen was determined using kit which was obtained from TEClot Fib Kit 10 Catalog No: 050-500, manufactured by TECO GmbH, Dieselstr. 1, 84088 Neufahrn NB Germany (Kumar and Sivakanesan, 2008).

All chemicals of analytical grade were obtained from Sigma-Aldrich Company, New Delhi.

3. Results

Anthropometric parameters in acute myocardial infarction (AMI) patients and control are shown in Table 1. Total cholesterol, its ratio to high density lipoprotein -cholesterol (TC/HDL-C) and triglyceride were significantly higher in both sexes of patients compared with control (Table 2 and 3). The low density lipoprotein –cholesterol (LDL-c) and its ratio to high density lipoprotein –cholesterol (LDL-c) (LDL-C/HDL-C) were higher in acute myocardial infarction (AMI) subjects than in control (Table-3). The behavioral pattern and familial history of cardiovascular disease is presented in Table 4. The distribution of risk factors and relative risk according to potential risk factors among cases and controls are presented in Table 5 and Table 6. The status of antioxidants and lipid peroxidation are shown in Tables 7. All antioxidants were significantly decreased in patients compared with controls. In agreement with this serum malondialdehyde (MDA) and conjugated diene (CD) were more abundant in patients compared with controls. Ischemia-modified albumin (IscMA) levels were also greater in both male and female patients compared with control (Table 7).Serum fibrinogen, caeruloplasmin, ischemia- modified albumin and C-reactive protein were significantly higher where as arylesterase activity were significantly lowered in cases compared with controls (Table 8).

	Control *(n=165)*	MI patients *(n=165)*	P- value (95%CI)
Age (years) 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 1. Anthropometric data of control and patients (mean ± SD)

Variables	*Controls (n=165)*	*Patients (n=165)*	*P-value (95%CI)*
Age	60.55 ± 3.98	61.84 ± 3.80	0.0037(61.26-62.42)
Total Cholesterol (mg/dl)	168.58 ± 12.16	186.44 ± 13.95	<0.001(184.31-188.56)
HDL-Cholesterol (mg/dl)	50.51 ± 6.78	41.27 ± 4.62	<0.001(40.56-41.97)
Triglycerides (mg/dl)	107.84 ± 11.51	128.96 ± 12.19	<0.001(127.10-130.82)
LDL-Cholesterol (mg/dl)	83.59 ± 11.95	119.37 ± 14.05	<0.001(17.22-21.51)
TC: HDL-C	3.39 ± 0.36	4.57 ± 0.58	<0.001(4.48-4.65)
LDL:HDL-C	1.90 ± 0.31	2.93 ± 0.51	<0.001(2.85-3.00)
TG: HDL-C	2.17 ± 0.35	3.16 ± 0.49	0.3149(3.086-3.234)

Table 2. Lipid profile in patients and healthy controls (mean ± SD)

Ratio	Controls (n=165)	Patients (n=165)
TC/HDL-C		
2-3	2.90 ± 0.09 (n=28)	-
3-4	3.44 ± 0.25 (n=129)	3.70 ± 0.20 (n=31)
4-5	4.19 ± 0.22 (n=8)	4.53 ± 0.27 (n=90)
5-6	-	5.26 ± 0.23 (n=44)
TG/HDL-C		
1-2	1.77 ± 0.13 (n=56)	-
2-3	2.38 ± 0.23 (n=109)	2.65 ± 0.27 (n=59)
3-4	-	3.42 ± 0.26 (n=99)
4-5	-	4.22 ± 0.19 (n=7)
LDL-C/HDL-C		
1-2	1.71 ± 0.17 (n=106)	1.86 ± 0.15 (n=5)
2-3	2.23 ± 0.21 (n=59)	2.57 ± 0.27 (n=81)
3-4	-	3.32 ± 0.21 (n=74)
4-5	-	4.11 ± 0.12 (n=5)

Table 3. Distribution of Lipid ratios in patients and healthy controls (mean ± SD)

		Control Group	Study Group
Hyperactive	*Yes*	39 *(23.63)*	68 *(41.21)*
	no	126 *(76.36)*	97 *(58.78)*
Triffle thinker *	*yes*	30 *(18.18)*	99 *(60.00)*
	no	135 *(81.81)*	66 *(40.00)*
Irrelevant thinker	*yes*	50 *(30.30)*	106 *(64.24)*
	No	115 *(69.69)*	59 *(35.75)*

Numbers in parentheses are percent unless mentioned otherwise
*Triffle thinker: subjects who thinks and worries on unnecessary small things

Table 4. Behavioral Pattern in AMI patients and control

	AMI Cases *(n=165)*	Controls (*n= 165)*
Age (y)	61.84 ± 3.80	60.55 ± 3.98
BMI (kg/m^2)	26.16 ± 1.45	25.40 ± 1.20
Waist-to-hip ratio	0.95 ± 0.11	0.93 ± 0.08[a]
Alcohol intake (servings/d)	0.36 ± 0.68	0.15 ± 0.34[a]
Physical activity (MET-min/d)	56.23 ± 123.8	97.83 ± 174.8[a]
Current cigarette smokers (%)	14.45	3.6[b]
Current bidi smokers (%)	23.67	12.31[c]
Family history of MI (%)	37.57	8.48[d]
Hypertension (%)	49.09	1.8[e]
Alcoholics (%)	47.87	20.60[f]

Values are in Mean ± SD
[a,b,c,d,e,f] Significantly different from cases (*t* test for matched data): [a,b,c] $P \leq 0.001$, [d,e] $P \leq 0.0001$, [f] $P \leq 0.003$

Table 5. Distribution of risk factors among AMI patients and control

	No. of cases *N*	No. of controls *N*	Age- and sex-adjusted RR (95% CI)[b]	Multivariate RR (95% CI)[c]
Cigarette smoking				
Never smoker	120	136	1.0	1.0
>10 cigarettes/d	36	6	7.8 (4.9, 13.5)	7.4 (4.3, 15.2)
Bidi smoking*				
Never smoker	120	136	1.0	1.0
> 10 bidis/d	49	8	8.2 (5.2, 14.2)	6.5 (3.9, 12.9)

BMI (kg/m²)				
20-24.9	30	51	1.0	1.0
≥ 25	135	114	2.7 (1.8,4.1)	2.9 (1.6, 5.1)
Waist –to-hip ratio				
≤ 0.95	52	137	1.0	1.0
> 1.0	113	28	3.9 (2.1, 6.3)	2.8 (1.6, 5.7)
Family history of MI				
No	97	151	1.0	1.0
Yes	62	14	2.1(1.6, 2.7)	2.7 (1.8, 3.8)
History of Hypertension				
No	136	142	1.0	1.0
Yes	29	23	2.1 (1.7, 3.2)	1.9 (1.4, 2.9)
Education level				
Highest level of education	25	27	1.0	1.0
None	101	132	3.1 (1.3, 5.1)	3.6 (1.0, 6.2)
Type of Family				
Split	20	64	1.0	1.0
Joint	145	101	4.5 (1.5- 2.9)	3.9(1.2-2.6)
Civil Status				
Lower Class	10	19	1.0	1.0
Middle Class	119	131	3.4 (4.3, 6.7)	2.8 (3.7, 5.9)
Higher Class	36	15	4.7 (4.9, 7.2)	3.8 (3.1, 4.7)
Leisure –time exercise				
Non-exerciser	82	58	1.0	1.0
≥ 145 MET-min/d	83	107	0.76 (0.4, 0.8)	0.68 (0.4, 0.7)
Household income				
>10 000 rupees/month	155	146	1.0	1.0
<5000 rupees/month	10	19	1.8 (1.2, 2.7)	1.7 (1.0, 3.1)
Hindu religion				
No	33	12	1.0	1.0
Yes	132	153	0.8 (0.6, 1.1)	0.9 (0.7, 1.3)

[a] MET, metabolic equivalent. RR estimates were obtained by using conditional logistic regression analysis controlled for the matching factors (age, sex, and hospital) and then additional potential risk factors.

[b] Also adjusted for hospital.

[c] Covariates controlled for in the multivariate model were as follows: age; sex; hospital; cigarette smoking never, current (≤10 cigarettes/d, >10 cigarettes/d)]; bidi smoking [never, current (≤10 bidis/d, >10 bidis/d)]; BMI, in kg/m² (20-24.9, ≥25); waist-to-hip ratio (≤0.95, >1.0); leisure time physical exercise (none, < 145 MET-min/d, ≤145 MET-min/d); history of hypertension (no, yes); history of diabetes (no, yes); history of high cholesterol (no, yes); family history of IHD (no, yes); education (none, primary school, middle, secondary, higher secondary, college, graduate or professional); household income (<5000, 5000-10000, 10000-15000,>10000 rupees/mo); and Hindu religion (no, yes).

[*] Bidis (pronounced bee-dees) are small hand-rolled cigarettes manufactured in India and other southeast Asian countries. They are exported to as many as 122 countries, according to one bidi manufacturer. Bidi cigarettes are made of tobacco wrapped in tendu or temburni leaf *(Diospyros melanxylon)*.

Table 6. Relative risk (RR) of Acute Myocardial Infarction (AMI) according to potential risk factors[a]

	Control *(n=165)*	AMI patients *(n=165)*	P value (95%CI)
Serum albumin (mg/dl)	4.4 ± 0.3	4.2 ± 0.3	<0.001(4.17-4.28)
Serum uric acid (mg/dl)	5.8 ± 1.2	4.3 ± 0.9	<0.01(4.18-4.45)
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	<0.001(0.62-0.69)
Serum superoxide dismutase (U/gHb)	1826.5 ± 31.9	813.9 ± 208.9	<0.02 (784.42-843.37)
Serum glutathione peroxidase (U/gHb)	61.3 ± 3.9	42.6 ± 6.3	<0.001(41.71- 43.48)
Serum catalase (k/gHb)	256.2 ± 26.7	193.1 ± 35.9	<0.001(188.03-198.16)
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	<0.02(11.55-15.06)
Serum conjugated dienes (µmol/L)	31.0 ± 2.7	48.3 ± 5.5	<0.001(47.44-49.11)

Table 7. Antioxidant status and Lipid Peroxidation in Control and AMI patients (mean ± SD)

	Control *(n=165)*	AMI 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)

Table 8. Other Biochemical parameters in Control and AMI patients (mean ± SD)

4. Dicussion

Coronary artery disease (CAD) remains the major cause of morbidity and mortality in all developed and developing countries in the world including India (Reddy and Yusuf, 1998). Dyslipidemia is one of the major modifiable risk factors for CAD (Chopra *et al*, 1998; Vasisht *et al*, 2000; Malhotra *et al*, 2003).

The coronary artery disease (CAD) 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 (Mishra *et al*, 2005). The search for various conventional risk factors among Asians could be helpful in recognizing the future events of stroke. These curiosities prompted us to identify the newer risk factors, with respect to Indian population.

The search for the newer risk factors continues and researchers are investigating the role of inflammatory markers and other potential risks factors which could link with acute myocardial infarction (AMI).

In this prospective case-control study in India, 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. The subjects selected for the study comprised of 165 controls, 48-69 y and 165 acute MI patients, 48-69 y.

Anthropometric variables in acute myocardial infarction (AMI) patients showed highly significant differences in waist/hip ratio and biceps skin fold thickness. Study reported (Heitman *et al*, 2004) 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*, 1999 also reported high hip circumference relative to weight and waist circumference is 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 the prevalence of obesity is minimal (Megnien *et al*, 1999). 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 control.

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 better tool for indentifying the future risk of acute myocardial infarction (AMI) in subjects by non-invasive procedures.

Observations of 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 acute myocardial infarction (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 control (1.9).

Earlier studies in lipid profile analysis conducted on acute myocardial infarction patients (Mishra *et al*, 2001; Das *et al*, 2002; Goswami *et al*, 2003; Kharb *et al*, 2003; Malhotra *et al*, 2003; Burman *et al*, 2004; Rajashekhar *et al*, 2004; Sivaraman *et al*, 2004; Rani *et al*, 2005; Shindhe, *et al*, 2005; Yadhav *et al*, 2006; Patil *et al*, 2007) 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 was observed in the present study. The present study concludes the importance of assessing the lipid ratios even in normolipidaemic 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 (MI) and coronary artery disease (CAD) 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.

Study conducted (Olusi *et al*, 1999; Djousse *et al* 2003) in acute myocardial infarction patients, reported significantly lower ($p<0.0001$) albumin and bilirubin ($p<0.0001$), where as lower levels of uric acid (Jing *et al*, 2000; Brand *et al*, 1985; Niskanen *et al*, 2004) and ascorbic acid (Nyossen *et al*, 1997; Bhakuni *et al*, 2006; Das *et al*, 2002; Kurl *et al*, 2002) in acute myocardial infarct patients were reported.

The aforementioned studies suggested 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 well established antioxidant, but at times it can also act as a pro-oxidant, which might increase the risk of myocardial infarction. Aulinskas *et al*, (1983) 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 (AMI) 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 to earlier studies (Senthil *et al*, 2004; Bhakuni *et al*, 2006; Jain *et al*, 2000; Rajashekhar *et al*, 2004; Das *et al*, 2002; Gupta *et al*, 2006; Patil *et al*, 2007) where lower activities of superoxide dismutase, catalase and glutathione peroxidase. Studies conducted (Senthil *et al*, 2004; Shindhe *et al*, 2005; Rajasekhar *et al*, 2004; El-Badry *et al*, 1995; Gupta *et al*, 2006 and Kharb 2003) 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 (Burman *et al*, 2004; Guha *et al*, 2001; Bal *et al*, 2001; Rajashekhar *et al*, 2004) also observed higher Lipoprotein (a) in AMI patients where as Nascetti *et al*, (1996) did not observed any change in Lipoprotein (a) levels in cardiovascular disease (CVD) patients and concluded lipoprotein (a) not to be considered as an independent risk factor in cardiovascular disease (CVD) patients.

Studies conducted (Senthil *et al*, 2004; Das *et al*, 2002; Kharb 2003; Bhakuni *et al*, 2006; Shindhe *et al*, 2005; Gupta *et al*, 2006) reported higher levels of malondialdehyde (MDA) in myocardial infarct patients.

Other biochemical parameters

The levels of caeruloplasmin, C-reactive protein, fibrinogen, ischemia-modified albumin were higher and arylesterase activities were lowered in patients. Studies conducted (Grobusch *et al*, 1999; El-Badry *et al*, 1995; Giurgie, 2005; Awadallah *et al*, 2006) observed significantly higher ($p<0.001$) levels of caeruloplasmin where as (Berton *et al*, 2003; Bhagat *et al*, 2003; Sivaraman *et al*, 2004; Kulsoom *et al*, 2006; Boncler *et al*, 2006) observed higher levels of C-reactive protein in patients. Shukla *et al*, (2006) stated elevated levels of caeruloplasmin as a risk factor for acute myocardial infarct patients. The reactive oxygen species disrupts copper binding to caeruloplasmin thus impairing its antioxidant property and further promoting oxidative pathology. Studies conducted on plasma fibrinogen levels in acute myocardial infarct patients (Harkut *et al*, 2004; Coppola *et al*, 2005; Beg *et al*, 2007; Sivaraman *et al*, 2004) reported rise in plasma fibrinogen as the present study. Earlier study conducted (Chawla *et al*, 2006; Auxter, 2003; Bar-Or *et al*, 2001) in acute myocardial infarct patients also reported higher levels in patients as observed by the present study. Studies on arylesterase activities in acute myocardial infarct patients (Aviram *et al*, 1999; Ayub *et al*, 1999; Richard *et al*, 2000; Jarvik *et al*, 2002; Azizi *et al*, 2002; Singh *et al*, 2007; Sarkar *et al*, 2006) also observed lower activities as concurrent to the current study. Increased C-reactive protein (CRP) concentrations in patients with unstable angina and acute myocardial infarct 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 (Pepys and Hirschfield, 2003).

Our study concluded apart from lipid profile, other variables which could be a probable risk for the future myocardial events have to be equally monitored. It is also recommended to increase dietary antioxidant intake in persons who already have known risk factors so that to some extent the myocardial infarction could be delayed. It is also important to check inflammatory markers like c-reactive protein and ischemia-modified albumin in a regular period of time after stepping early forties as they could be a cost effective mode of diagnosis and the subjects can be efficiently monitored and complications of myocardial infarction can be prolonged.

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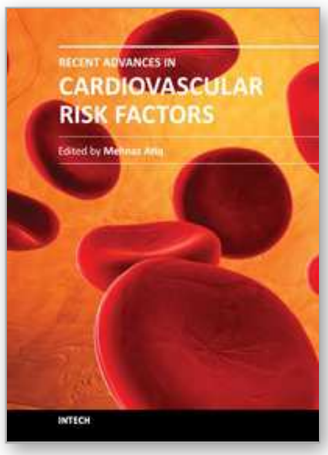

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Among the non-communicable diseases, cardiovascular disorders are the leading cause of morbidity and mortality in both the developed and the developing countries. The spectrum of risk factors is wide and their understanding is imperative to prevent the first and recurrent episodes of myocardial infarction, stroke or peripheral vascular disease which may prove fatal or disabling. This book has tried to present an update on risk factors incorporating new research which has thrown more light on the existing knowledge. It has also tried to highlight regional diversity addressing such issues. It will hopefully be resourceful to the cardiologists, general practitioners, family physicians, researchers, graduate students committed to cardiovascular risk prevention.

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