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Original Research Paper

Cardiology

EPIDEMIC OF CAD IN YOUNG INDIANS : THE ACCELERATED ATHEROSCLEROTIC INSULIN RESISTANCE SYNDROME (AAIRS)

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ABSTRACT

Introduction: CAD is the leading cause of mortality in India. It affects Indians atleast a decade early compared to the western population. Other than the conventional risk factors, the prevalence of other risk factors like hyperhomocystenemia, lipoprotein(a), metabolic syndrome, insulin resistance and fatty liver was studied in a large registry of documented CAD in patients. **Objectives:** To study the prevalence of insulin resistance syndrome and its association with NAFLD, lipoprotein (a) and homocysteine levels in young Indian patients who present with coronary artery disease. **Materials and Methods:** It is a single centre prospective sub study of the PCAD (Premature coronary artery disease) registry cohort at Jayadeva Institute. **Results**: 344 patients and 300 controls were studied. The mean age was 32 years. There were 45 females and 299 males in cases, 99 females and 201 males in control group. Smoking was seen in 138 cases compared to 16 controls which was disproportionately high in the cases group. 8% of cases had diabetes whereas only 1.6% of controls had diabetes. 10% of cases had positive family history of CAD compared to 0 in control group. 68% of cases had metabolic syndrome whereas 36% of controls had metabolic syndrome. Elevated serum homocysteine levels were seen in 49 when compared to 46 controls which was statistically significant. ($p < 0.001$). Homocysteine level more than 15 was seen in 68% of cases compared to 45% in controls which was statistically significant.Serum lipoprotein a levels was significantly higher in cases (mean of 52) compared to controls (mean of 26). Lp(a) level more than 30 was seen in 51% of cases compared to 27% of controls. HOMA IR was significantly high in the cases group when compared to controls which was statistically significant. Fatty liver grade 0 was seen in 25% of cases compared to 58% in controls. Fatty liver grade 1 was seen in 59% of cases compared to 37% in controls. Fatty liver grade 2 was seen in 15% of cases compared to 3.7% in controls, all were statistically significant. **Conclusion:** Novel syndrome of AAIRS incorporating insulin resistance, NAFLD, Lipoprotein a and homocysteine was found to be statistically different between cases and controls. Hence, this can be used to predict the risk of premature coronary disease in young Indians **Aims:** To formulate a novel clinical syndrome titled Accelerated Atherosclerosis Insulin Resistance Syndrome (AAIRS) which will help to predict the risk of premature coronary heart disease in young Indians **Objectives:** To study the prevalence of insulin resistance syndrome and its association with NAFLD, lipoprotein (a) and homocysteine levels in young Indian patients who present with coronary artery disease

KEYWORDS :

INTRODUCTION:

Coronary artery disease (CAD) has become a leading cause of morbidity and mortality in India and worldwide [1,2]. By 2020 India will be the cardiovascular disease capital of the world.

The risk of CAD in Indians is 3-4 times higher than White Americans, 6-times higher than Chinese, and 20-times higher than Japanese[1,4]. Indians are prone as a community to CAD at a much younger age[5,6].

Premature CAD is defined as cardiac events occurring before the age of 55 in men and 65 in women. In its severe form it is defined as CAD occurring below the age of 40 years.

CAD is affecting Indians 5-10 years earlier than other communities. In the Western population, incidence of CAD in the young is up to 5% as compared to 12-16% in Indians[9,10]. The average age of 1st heart attack in Indians is 10 yrs younger compared to western population, and 25% of 1st heart attacks are occurring before the age of 40yrs.

Epidemiological studies (largely cross-sectional surveys) from various parts of India have reported the rising trends and a high burden in the levels of conventional risk factors such as diabetes, hypertension and insulin resistance syndrome which are largely determined by urbanization as evident from the urban-rural difference in the risk factors observed in India[11]

Several definitions of metabolic syndrome are available; initially by the World Health Organization (WHO)[30], and later by Expert Committee of National Cholesterol Education Program (NCEP, Adult Treatment Panel III)[31] and by others[32]. However, ambiguities have been identified in these definitions.

First, although insulin resistance is the central patho physiological feature of metabolic syndrome, a direct or surrogate measure of insulin resistance has not been included as one of the defining variable in the NCEP definition.

Second, the cut-off points of waist circumference (as included in NCEP definition) and body mass index (BMI) (as included in the WHO definition) have been defined using data from white Caucasians but are not suitable for Indians who have different anthropometric measurements. Investigations of these issues would lead to optimal definition of metabolic syndrome in Asian Indians and pave way for rational application of population-based preventive strategies.

Nonalcoholic fatty liver disease (NAFLD) is quite prevalent in South Asians and is an important hepatic correlate of insulin

resistance and the Metabolic Syndrome, with non-alcoholic steatohepatitis often being the first clinical indication of insulin resistance. Both obese and non-obese Indians with NAFLD have significantly higher insulin resistance compared to those without NAFLD. An Indian study reported the presence of early abnormalities in hepatic gluconeogenesis pathway in nondiabetic obese and nonobese Asian Indians with NAFLD, indicating increased future risk for development of type 2 diabetes[33, 34].Non-conventional risk factors seem to play a very significant role in the pathogenesis of CAD in Asian Indians. Therefore, these can be considered the conventional risk factors for this population. Elevated homocysteine and lipoprotein (a) [LP(a)] levels have a direct association with accelerated CAD[1].

On April 1st 2017, a first-of-its-kind Registry/clinic/research centre was started in our centre exclusively for Premature CAD (males < 40yrs, females < 45yrs) under the title of Project PCAD. This was to study the incidence , prevalence, clinical profile and to study the uniqueness of Indians which predisposes them to PCAD. Within 3 months we had a massive number of 400 patients registered.

Review of literature:

Reaven initially proposed that the coexistence of obesity, glucose intolerance, dyslipidemia, and hypertension be termed *insulin resistance syndrome* (metabolic syndrome, syndrome X)[35].

Investigators have described a relationship between markers of insulin resistance (such as hyperinsulinemia) and an increase in the risk of CVD risk [36,37]. The Quebec Cardiovascular Study[37] described an association between increased fasting blood insulin concentration (as a surrogate measure of insulin resistance) and an increased risk of ischemic heart disease. Hyperinsulinemia was found to be an independent risk factor for CAD. Thus, elevated fasting insulin was an independent predictor of ischemic heart disease events even in this population without diabetes [37]. Insulin resistance is synergistic with dyslipidemia in increasing risk. Data from the San Antonio Heart Study [54] suggest that insulin resistance per se is linked to the risk for macrovascular disease in normoglycemic subjects who subsequently develop diabetes. Data from the Insulin Resistance Atherosclerosis Study [38] demonstrate that reduced insulin sensitivity is associated with an increase in the severity of atherosclerosis [39].

The increasing prevalence of the insulin resistance syndrome and its strong association with risk of CAD underscore the potential importance of its early diagnosis and aggressive treatment.

Several definitions of metabolic syndrome are available; initially by the World Health Organization (WHO) [30], and later by Expert Committee of National Cholesterol Education Program (NCEP, Adult Treatment Panel III)[31] and by others[32]. However, ambiguities have been identified in these definitions.

First, although insulin resistance is believed by many investigators to be the central pathophysiological feature of metabolic syndrome, the NCEP definition has rarely been scientifically correlated against measures of insulin resistance in population-based studies and direct or surrogate measure of insulin resistance has not been included as one of the defining variable in the NCEP definition.

Second, the cut-off points of waist circumference (as included in NCEP definition) and body mass index (BMI) (as included in the WHO definition) have been defined using data from white Caucasians but are not suitable for Asian ethnic groups who have different anthropometric characteristics [43-45]. For defining overweight in Asian populations, a cut-off point of 23 kg/m2 instead of 25 kg/m2 has been suggested 25, since the increased risk for morbidities such as type 2 diabetes mellitus (T2DM) and hypertriglyceridemia manifest at a lower range of BMI (22–25 kg/m2) [46]. Also, investigators opine that lower cut-off points of waist circumference for defining abdominal obesity might be more suitable for Asians than those suggested by NCEP [47,48].Overall, Asians are shorter and thinner than white Caucasians and most of them would be considered non-obese by the currently accepted criteria but they have abdominal adiposity [49,50]. Importantly, insulin resistance is widely prevalent in Asian Indians and its magnitude is higher than white Caucasians, substantially contributed by anthropometric features[51,52].

Therefore, it appears that the current definitions might not be appropriate for identifying Asian Indians with insulin resistance syndrome. Metabolic abnormalities associated with insulin resistance are known to occur during the childhood and adolescence that may increase the risk of T2DM in adults. It is important to characterize and prevent metabolic syndrome in Asian Indians at a young age, since this ethnic group is highly predisposed to develop insulin resistance, T2DM, and coronary heart disease. Identification and the prevalence of metabolic syndrome, and its correlation with fasting hyperinsulinemia are important issues that have not been investigated in young Indians presenting with coronary artery disease. Investigations of these issues would lead to optimal definition of metabolic syndrome in Indians and paveway for rational application of population-based preventive strategies. Non alcoholic fatty liver disease (NAFLD) is quite prevalent in South Asians and is an important hepatic correlate of insulin resistance and the MetS, with non-alcoholic steatohepatitis often being the first clinical indication of insulin resistance[7]. Both obese and non-obese Indians with NAFLD have significantly higher insulin resistance compared to those without NAFLD. An Indian study reported the presence of early abnormalities in hepatic gluconeogenesis pathway in nondiabetic obese and nonobese Asian Indians with NAFLD, indicating increased future risk for development of type 2 diabetes[48,49].Non-conventional risk factors seem to play a very significant role in the pathogenesis of CAD in Asian Indians. Therefore, these can be considered the conventional risk factors for this population. Elevated homocysteine and lipoprotein (a) [LP(a)] levels have a direct association with accelerated CAD[54]

MATERIALS AND METHODS:

It is a single centre prospective sub study of the PCAD (Premature coronary artery disease) registry cohort being carried out at our institute which is a 600 bed tertiary level dedicated cardiac centre in Bengaluru.

Our study included 344 patients and 300 controls. All cases were selected according to predetermined inclusion and exclusion criteria.

The Medical Ethics Committee approval was obtained and written informed consent was taken from all patients. Patients were asked to complete a health questionnaire covering medical history, risk factors, smoking habits and medical treatment. A standardised diagnostic protocol was followed consisting of physical examination and laboratory testing in a fasting state. Controls chosen were asymptomatic and had normal ECG and Echocardiography.

The selection criteria for cases include :

Inclusion Criteria :

(a) Men aged 40 years old or younger .
(b) Women aged 45 years old or younger

(c) All patients with diagnosis of Ischemic heart disease , as evidenced by :
- Documented Acute coronary syndrome (Unstable angina , ST elevation / Non ST elevation myocardial infarction)
- Chronic stable angina with evidence of coronary artery disease

(d) Conventional risk factors like smoking.

Exclusion Criteria :

(a) Patients having a history of chronic alcoholism, concomitant liver, or kidney disease and acute or chronic infection

(b) Patients taking hypolipidemic drugs, oral contraceptives, or hormone replacement therapy

© Patients unwilling to give informed consent

Definitions

The **metabolic syndrome** was defined according to the Adult Treatment Panel III (ATPIII) criteria of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood.

Subjects were diagnosed with the metabolic syndrome if three or more of the following abnormalities were present:

(1) Abdominal obesity: waist circumference >90 cm in men or >80 cm in women.

(2) High blood pressure: >130 mm Hg systolic or >85 mm Hg diastolic or use of blood pressure lowering agents.

(3) Hypertriglyceridaemia: serum triglycerides >1.70 mmol/l (150 mg/dl).

(4) Low HDL-cholesterol: serum HDL- cholesterol ,1.04mmol/l (40 mg/dl) in men or ,1.29 mmol/l (50 mg/dl) in women.

(5) High fasting glucose: fasting serum glucose >6.1 mmol/l (100 mg/dl) or use of glucose lowering agents. Diabetes mellitus is defined as the use of glucose lowering agents and/or a fasting serum glucose concentration >7.0 mmol/l.

Smoking and alcohol consumption are defined as smoking or use of alcohol within the last 12 months. Creatinine clearance (ml/min) was estimated by the CockroftGault formula. Insulin resistance (IR) at baseline was estimated using the homeostasis model assessment (HOMA-IR) method using the formula: HOMA-IR (mmol/L × μIU/ml) = fasting glucose (mmol/L) × fasting insulin (μIU/ml)/22.5

Clinical profile and measurements:

The anthropometric and body composition data (waist circumference [WC], hip circumference, body mass index [BMI], waist-to-hip circumference ratio [W–HR] and blood pressure will be assessed

Metabolic parameters:

The laboratory procedures; estimation of fasting blood glucose (FBG), total cholesterol (TC), serum triglycerides (TG), and high-density lipoprotein cholesterol (HDL-c) , Lp(a) and low-density lipoprotein cholesterol (LDL-c) along with homocystiene levels will be carried out. Serum insulin levels will be determined.

The intra-assay and inter-assay percentage coefficient variables will be formulated. The quality control check on insulin assays will be rigorously maintained by a biochemist. Fatty liver will be assessed by abdominal ultrasound. Intra group comparisons will be done between those who have increased fasting insulin levels and those without.

Utrasound of abdomen was done to look for fatty liver. Steatosis is graded as follows: Absent (score 0) when the echotexture of the liver is normal; mild (score 1), when there is a slight and diffuse increase of liver echogenicity with normal visualization of the diaphragm and of the portal vein wall; moderate (score 2), in case of a moderate increase of liver echogenicity.

Sample Size:

344 patients with premature CAD with no evidence of metabolic syndrome and conventional risk factors like smoking and diabetes, 300 controls

Study Design: prospective descriptive study.

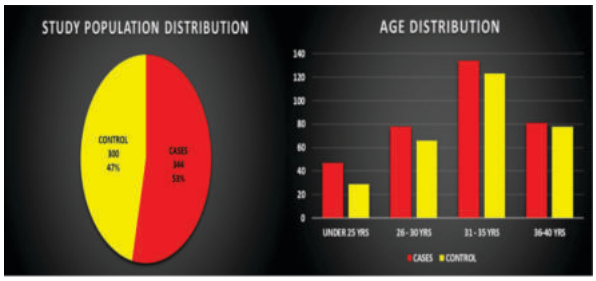
Sampling technique: Systematic random sampling

Statistical methods:

Chi-Square test, Fisher exact test, student t test, any other suitable method at the time of data analysis

RESULTS:

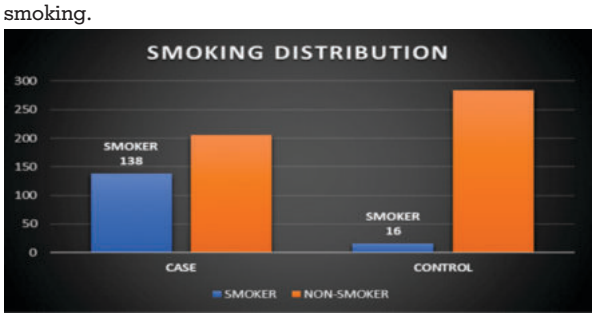
344 patients and 300 controls were considered for this study. The mean age of the study population was 32 years. There were 45 females and 299 males in cases, 99 females and 201 males in control group. Majority of the cases and controls were in the 31-35yrs group as shown below.



Gender distribution: 13 percent of cases were female and 33 percent of controls were female.

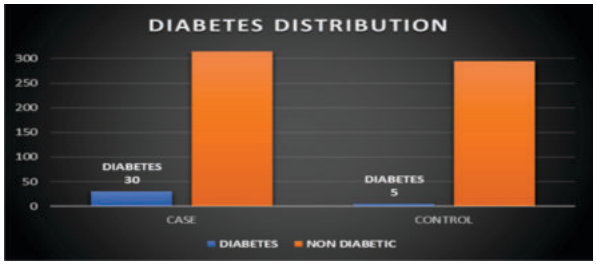
Risk factors profile:

Traditional risk factors like smoking, diabetes and family history of CAD was evaluated. Smoking was seen in 138 cases compared to 16 controls which was disproportionately high in the cases group. 40% of patients with premature CAD had history of smoking whereas only 5% of controls had history of smoking.



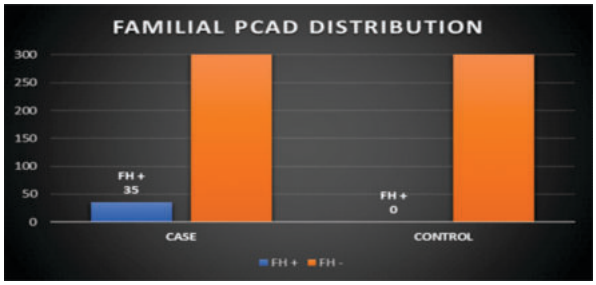
Prevalence of diabetes:

It was seen in 30 cases and 5 controls. 8% of cases had diabetes whereas only 1.6% of controls had diabetes.



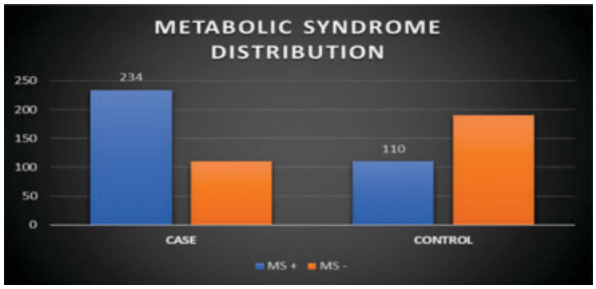
Family history of CAD:

It was seen in 35 cases when compared to 0 controls. 10% of cases had positive family history of CAD compared to 0 in control group.



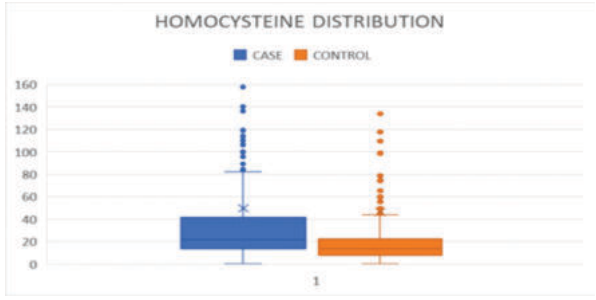
Metabolic syndrome:

234 cases with CAD had metabolic syndrome. 68% of cases had metabolic syndrome whereas 36% of controls had metabolic syndrome.



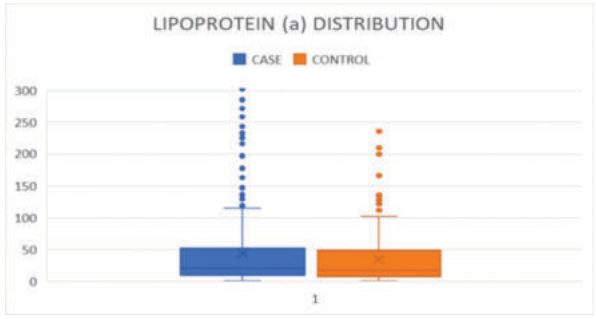
Serum homocysteine levels:

Elevated serum homocysteine levels were seen in the cases (mean of 49) when compared to controls (mean of 46) which was statistically significant. (p value of <0.001). Homocysteine level more than 15 was seen in 68% of cases compared to 45% in controls which was statistically significant.



Serum lipoprotein α levels:

It was significantly higher in cases (mean of 52) compared to controls (mean of 26). Lp(α) level more than 30 was seen in 51% of cases compared to 27% of controls.



Insulin resistance:

It was measured by calculating HOMA IR levels using fasting insulin and fasting glucose levels. HOMA IR was significantly high in the cases group when compared to controls which was statistically significant.

Group	N	Mean	SD	P value (t test)	P(Mann Whitney test)
CASE	344	215.2	905.0	0.003	<0.001
CONTROL	300	65.4	132.7		

Table 1(a): Univariate analysis

Variable	Group	N	Mean(SD)	Median(IQR)	P-value (t-test)	P-value (Mann-Whitney)
Age	CASE	344	32.16(5.63)	33(28,35)	0.487	0.751
	CONTROL	300	32.45(4.97)	33(30,36)		
Homocysteine	CASE	344	49.79(299.16)	22.11(13.51,41.06)	0.912	<0.001
	CONTROL	300	46.35(462.11)	13.48(8.03,22.26)		
Lp(α)	CASE	344	52.3(54.55)	31.35(17.17,70)	<0.001	<0.001
	CONTROL	300	26.55(26.61)	16.5(7.4,35.33)		

Fatty liver:

Presence of fatty liver was detected by ultrasonography of abdomen. Fatty liver was graded as follows: Absent (score 0) when the echotexture of the liver is normal; mild (score 1), when there is a slight and diffuse increase of liver echogenicity with normal visualization of the diaphragm and of the portal vein wall; moderate (score 2), in case of a moderate increase of liver echogenicity. Fatty liver grade 0 was seen in 25% of cases compared to 58% in controls. Fatty liver grade 1 was seen in 59% of cases compared to 37% in controls. Fatty liver grade 2 was seen in 15% of cases compared to 3.7% in controls, all were statistically significant.

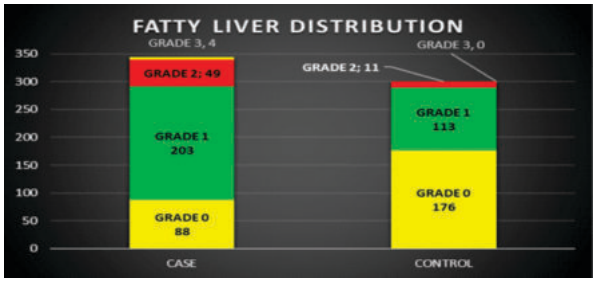


Table 1(b): Univariate analysis

Levels	CASE	CONTROL	Pvalue
Female	45(13.1)	99(33)	<0.001
Male	299(86.9)	201(67)	
Homocysteine<15	108(31.4)	164(54.7)	<0.001
Homocysteine>15	236(68.6)	136(45.3)	
Lp(α)<30	167(48.5)	217(72.3)	<0.001
Lp(α)>30	177(51.5)	83(27.7)	
MS:No	110(32)	190(63.3)	<0.001
MS:Yes	234(68)	110(36.7)	
FL score: 0	88(25.6)	176(58.7)	<0.001
FL score: 1	203(59)	113(37.7)	
FL score: 2	53(15.4)	11(3.7)	

DISCUSSION:

Premature coronary artery disease in India is a health concern of importance due to the number of people getting affected by it. Apart from the traditional risk factors of smoking, diabetes and family history we explored other risk factors like insulin resistance, metabolic syndrome, hyperhomocysteinemia and increased lipoprotein (a) levels in this study.

Smoking was found to be significantly higher in cases compared to controls. It continues to be a very important risk factor in patients with premature CAD. Diabetes prevalence in both cases and controls was low in this study. Familial predisposition to coronary artery disease was high in cases (10%) compared to controls. Metabolic syndrome prevalance was higher in cases (68%). This is comparable with a study done in Indian population with angiographic proven CAD where metabolic syndrome was seen in 77% of patients.[1]

Elevated serum homocysteine levels has been studied as a risk factor for CAD in many studies.[2-5]. Hyperhomocysteinemia increases the risk of CAD by increased thrombosis, adverse effects on endothelial function, promoting thickening of the intima, increased platelets aggregation, and oxidative damage of low-density lipoproteins. Serum homocysteine levels were significantly higher in the cases group in our study.

In Veeranna et al, Hcy level (>15 µmol/l) significantly predicted CVD (adjusted hazard ratio [aHR]: 1.79, 95% confidence intervals [CI]: 1.19 to 1.95; p = 0.006) and CHD events (aHR: 2.22, 95% CI: 1.20 to 4.09; p = 0.01) in the MESA trial and CVD (aHR: 2.72, 95% CI: 2.01 to 3.68; p < 0.001) and CHD mortality (aHR: 2.61, 95% CI: 1.83 to 3.73; p < 0.001) in the NHANES III, after adjustments for traditional risk factors and C-reactive protein. [18]

In the Hordaland Homocysteine Study, plasma homocysteine level positively related to total cholesterol level, blood pressure, and heart rate and inversely related to physical activity. [19]

In another South Indian study done by Vijetha Shenoy et al, serum homocysteine was found to be higher in patients with CAD undergoing angiogram compared to controls. [20]

In our study, mean serum homocysteine levels were higher in cases compared to controls. Also level more than 15µmol/l which is considered significant in most of the studies was found in nearly 68% of cases which was staistically significant when compared to controls (45%).

Serum lipoprotein (a) has been studied as a risk factor in multiple studies. Lp(a) is involved in the development of atherothrombosis and activation of acute inflammation exerting a proatherogenic and hypofibrinolytic effect. Lp(a) plays a critical role in the proinflammatory reaction and can be considered as a common joint among different metabolic systems. Other actions of Lp(a) can be resumed as follows: inhibition of the activation of plasminogen; inhibition of the activation of TGF-β; activation of acute inflammation; induction of the expression of adhesion molecules; elevation of the production of cytokines. Moreover Lp(a) is implicated in the activation of endothelial uptake, oxidative modification, and foam cell formation, suggesting that these processes could play an important role in atherosclerosis.

In people of European descent, there is consistant relationship between Lp(a) of 20-30 mg/dl and CAD. As Lp(a) levels increase, risk also increases [17]

The INTERHEART Lp(a) study—by far the largest case–control study on Lp(a) and AMI—measured Lp(a) levels in a total of 12,943 subjects comprising 7 largest ethnic groups across the world. South Asians were well represented (n = 1829), with 948 cases and 881 age- and gender-matched controls. This study convincingly demonstrated that Lp(a) is an independent risk factor for AMI in diverse populations. South Asians had increased Lp(a) levels than whites (14 mg/dl *vs*. 10 mg/dl).Notably, the OR for AMI with elevated Lp(a) was the highest in South Asians and more than double that of whites (OR 2.14 *vs* 1.36 $p < 0.001$) [22]

In 2010, the European Atherosclerosis Society recommended an Lp(a) high-risk threshold of >50 mg/dl (125 nmol/L), which represented the 80th percentile for the European population.[23] In 2018, the National Heart, Lung, and Blood Institute (NHLBI) endorsed an Lp(a) high-risk range of >30–50 mg/dl (75–125 nmol/L) to accommodate the implications of more recent studies.[24]In the Framingham Heart Study, the 75th percentile of Lp(a) distribution was 30 mg/dl and 90th percentile was 38 mg/dl. [25] Most epidemiologic and case–control studies that measured Lp(a) in fresh plasma as well as an updated review of epidemiological and MR studies from Copenhagen population have shown a risk range of 20–30 mg/dl. This new analysis included 58,340 subjects, measured Lp(a) in fresh samples using isoform-insensitive assays, corrected for regression dilution bias, recorded 1897 validated AMI, and also focused on those with extremely high Lp(a) levels.

For any given level of cholesterol and LDL-C, Indians have a greater risk of CAD, at least in part due to the substantial enrichment of LDL with Lp(a), which is included in the calculated LDL reported by the laboratory. Because of the heightened risk conferred by Lp(a) in South Asians, an Lp(a) threshold of >30 mg/dl (75 nmol/l) should be considered high and >50 mg/dl (>125 nmol/l) should be considered very high. An estimated 25% of South Asians have Lp(a) >50 mg/dl, compared with <10% having diabetes. While awaiting the availability of Lp(a)-lowering therapies, high-intensity statin therapy to ultralow LDL-C should remain the mainstay of management of elevated Lp(a) levels.

The LOLIPOPS, by far the largest prospective study of South Asians to date, has demonstrated a twofold incidence of CAD compared to whites, adjusted for established risk factors and emerging risk factors. The LOLIPOPS investigated the reasons for the higher susceptibility of Indians to CVD compared to Europeans by prospectively following up a large cohort with oversampling of South Asian men and women (South Asians 16,774; whites 7032). Compared to Europeans, the odds ratio (OR) for the incidence of CAD in South Asians after adjustment for age and gender was 2.55 (2.26–2.87, $p <$ 0.001), which increased to 2.67 (2.33–3.06 $p < 0.001$) after adjustments for cholesterol and smoking. The OR decreased to 2.28 (1.97–2.63 $p < 0.001$), when adjustments were made for obesity, abdominal obesity, hypertension, and diabetes. Further adjustments for homeostatic model assessment insulin resistance, triglycerides, and high density lipoprotein (HDL) decreased the OR to 1.81 (1.54–2.11, p 0.001). This largest prospective study of South Asians has confirmed a nearly twofold higher incidence of CAD compared to Europeans at all age groups.[21]

In our study, HOMA IR was significantly high in cases when compared to controls. When association was studied between insulin resistance and other risk factors, strong association between insulin resistance and hyperhomocysteinemia and fatty liver was noted which was statistically significant. (P<0.001). Srinivasan et al. studied 61 T2DM who were submitted to coronary arteriography in a cross-sectional study. The log-HOMA-IR was positively associated with the severity of coronary risk[27]. Similar results were obtained in the San Antonio Heart Study which found a significant association between HOMA-IR and risk of CVD after adjustment for multiple covariates[28]. In a large observational study, Hedblad B et al. [29]studied normoglycemic individuals without previous cardiovascular events who were divided according to the presence or not of insulin-resistance on the basis of the 75th percentile of HOMA-IR and followed for 6 years. They found that individuals with HOMA-IR above the p75 had a twice increase in relative risk for cardiovascular events and death.

CONCLUSION:

Novel syndrome of AAIRS incorporating insulin resistance, NAFLD, Lipoprotein a and homocysteine was found to be statistically different between cases and controls. Hence, this can be used to predict the risk of premature coronary disease in young Indians.

Limitations:

It was a single center study predominantly involving urban population from South India. We need larger multicentric studies to generalise these results to rest of the population.

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