

A Study of Measurement of ASCVD Risk Parameters in Patients with Clinical Atherosclerotic Cardiovascular Disease

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Received: May 02, 2019; Accepted: May 09, 2019; Published: May 16, 2019

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Abstract

Objectives: To measure Atherosclerotic Cardiovascular Disease (ASCVD) risks and parameters in patients with clinical ASCVD.

Materials and methods: This retrospective study was conducted in Cardiology Department of KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, a tertiary care center situated in North Karnataka, Belagavi, India. Data was collected from January 2018 to December 2018. A total 952 patients with clinical ASCVD aged >40 years who were on statin therapy were included in the study. The records of patients with ASCVD were evaluated for risk parameters based on ACC AHA cholesterol guidelines 2018.

Results: Out of 952 patients, consisting of 77% of the patients were males and 23% were females. The mean age was 62.45 ± 8.18 years. Most of the patients (43.7%) were aged between 61 to 70 years. Overall 51.37% of the patients had positive history of hypertensive treatment, followed by history of diabetes mellitus, prior revascularization, smoking, Congestive cardiac failure (CCF) and chronic kidney disease (CKD). None of the patient had heterozygous familial hypercholesterolemia. With regard to lipid abnormalities, majority of the patients (60.61%) had low high-density lipoprotein (HDL) followed by hypertriglyceridemia, elevated low-density lipoprotein (LDL) and hypercholesterolemia.

Conclusion: Most common risk factor for ASCVD is hypertension followed by diabetes, dyslipidemia and smoking. With incidence being higher in very high clinical ASCD compared to stable ASCVD.

Keywords: Atherosclerotic cardiovascular disease; Cardiovascular disease; Statin therapy

Introduction

Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of morbidity and mortality worldwide [1]. Economic development and industrialization promoted unhealthy diet and decreased physical activity which leads to Atherogenesis [2]. Atherosclerotic cardiovascular disease (ASCVD) accounts for approximately 17.7 million deaths annually, the majority of which are preventable [3]. About 1 in 3 American adults age 40 and older have hypercholesterolemia with total cholesterol levels of 200 mg/dL or higher [4]. The Center for Disease Control and Prevention (CDC) estimate that 78 million U.S. adults have an indication for statin therapy [5].

Atherosclerosis is the pathological process in the coronary arteries, cerebral arteries, iliac and femoral arteries, and aorta that is responsible for coronary heart disease (CHD), stroke, and peripheral arterial disease (PAD). It begins during childhood in the intima of the large elastic and muscular arteries with deposits of lipids, principally

cholesterol and its esters, in macrophages and smooth muscle cells. The lesions, called fatty streaks, produce only minimal intimal thickening and cause no disturbances in blood flow during early childhood, but they rapidly become more extensive during adolescence. In young adults, more lipid is deposited at some sites, and a core of lipid and necrotic debris becomes covered by a cap of smooth muscle and fibrous tissue. These changes produce elevated lesions called fibrous plaques that project into the lumen and begin to disturb blood flow [6].

One of the most important advances in medicine has been the identification of the major risk factors for CVD, which arose from large prospective cohort studies such as the Framingham Heart Study and the Seven Countries Study [7-9]. The major modifiable risk factors include elevated blood pressure, dyslipidemia, smoking, and diabetes mellitus. A substantial body of evidence now supports reducing these factors to reduce morbidity and mortality associated with ASVD. Indeed, screening for and treating these conditions forms the basis of many published guidelines of risk assessment and reduction strategies [7,10-12].

Use of statins in both primary and secondary prevention is a cornerstone for cardiovascular therapeutics [2]. The latest guidelines from the American College of Cardiology (ACC) and American Heart Association (AHA) recommend that for optimal ASCVD risk reduction the first-line therapies are adherence to a heart healthy lifestyle and consideration of evidence-based doses of 3-Hydroxy-3-MethylGlutaryl-Coenzyme A reductase inhibitors (HMG-CoA reductase inhibitors i.e., statins) based on 10-year ASCVD risk estimation and a clinician-patient risk discussion. Although statins are among the most commonly used pharmaceuticals in clinical practice with 200 million patients on this therapy worldwide, adherence to these cardiovascular morbidity and mortality-reducing medications has been challenging. One major limitation to statin adherence is the persistent concern about adverse effects largely from case reports. Given that statin therapy is a cornerstone of ASCVD prevention, it is essential for clinicians to understand statin safety issues and the available evidence supporting the incorrect perception that statins have common adverse effects [3]. However, the 2018 Scientific Statement from the American Heart Association provides a comprehensive analysis of the most up-to-date evidence of potential adverse effects and tolerability of statins [1]. From the totality of available evidence, it is prudent to advise patients who are recommended to take statin therapy that this therapy can provide a major benefit in risk reduction with infrequent risks. The adverse effects of statins are generally minor, and the majority of evidence does not support the misguided perception of frequent adverse effects. Improved awareness and recognition of the rarity of adverse effects with statin use among clinicians and patients will booster cardiovascular prevention efforts as well as support patient adherence to guideline-directed therapy [3]. Considering these facts, the present study was undertaken to measure ASCVD risk parameters in patients with clinical ASCVD.

Research Methodology

This retrospective study was conducted in Cardiology Department of KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, a tertiary care center situated in North Karnataka, Belagavi India. Data was collected from January 2018 to December 2018. A total 952 patients with clinical ASCVD aged >40 years who were on statin therapy were included in the study. Permission was obtained from Department of Medical Records (MRD) to retrieve the data of patients with ASCVD who attended Department of Cardiology from January 2018 to December 2018.

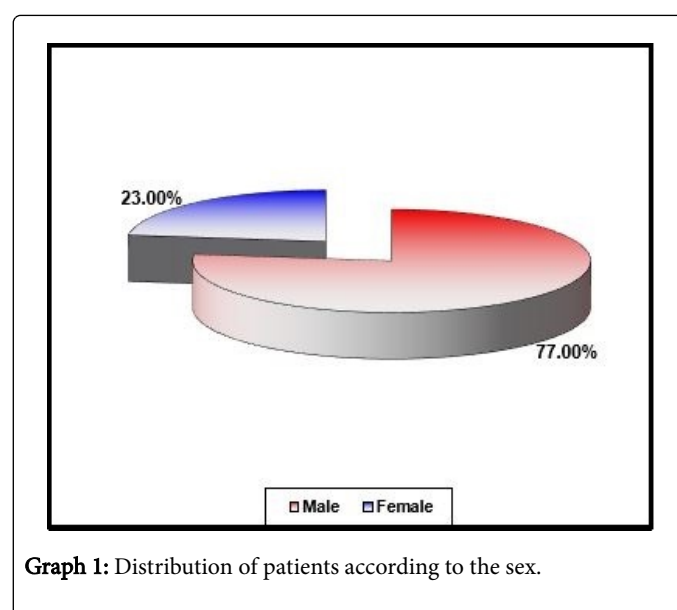
The records of patients with ASCVD were evaluated for risk parameters that included, Demographic characteristics, history of Hypertension and its treatment, history of diabetes mellitus, smoking status, CKD, history of prior revascularization, history of congestive cardiac failure, dose of statin therapy and lipid profile (that included total cholesterol, high density lipoprotein, low density lipoprotein and triglycerides). These observations were recorded on predesigned and pretested proforma.

Risk stratification of ASCVD patient was categorized as stable (High) and very high risk clinical ASCVD groups based on ACC AHA cholesterol guidelines 2018 [1]. The lipid profile was evaluated based on ACC AHA cholesterol guidelines 2018 guidelines [1].

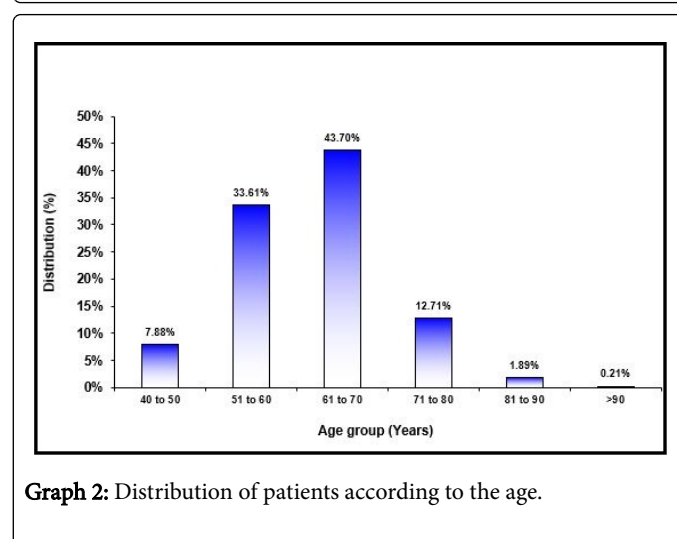
The data obtained was tabulated on Microsoft Excel spreadsheet. The data was analysed using SPSS statistical software version 20.0. The categorical data was expressed as ratios and percentages. The continuous data was expressed as mean \pm standard deviation (SD).

Results

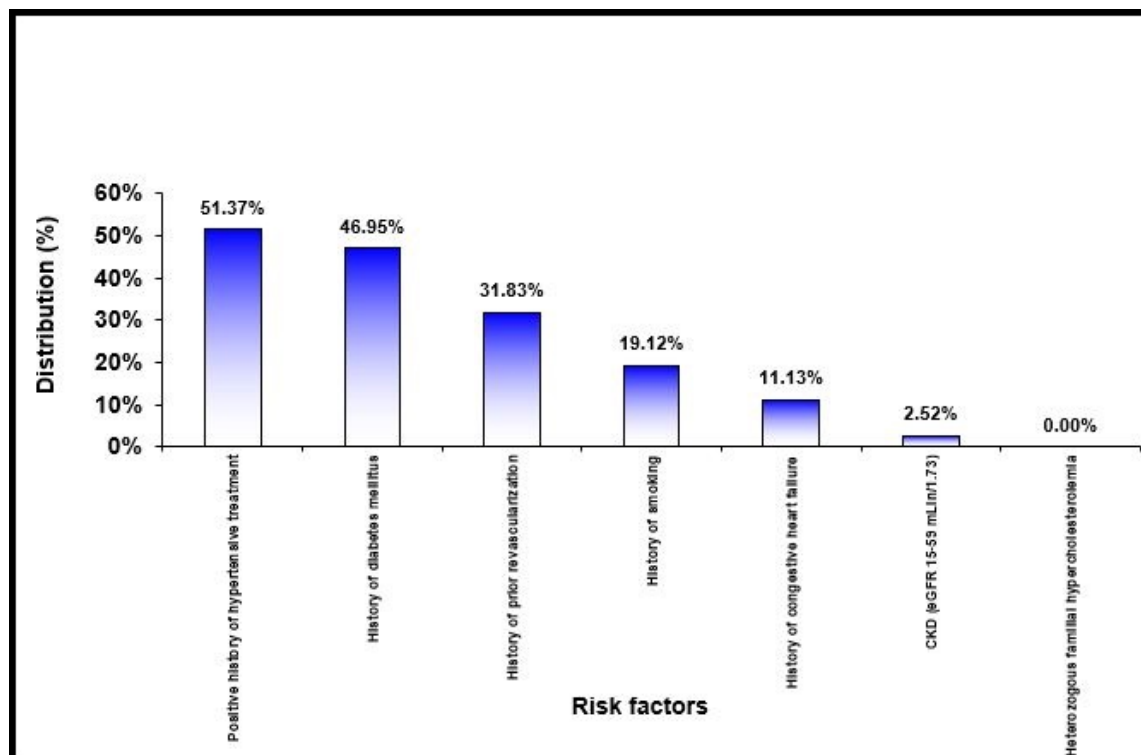
Out of 952 patients, consisting of 77% of the patients were males and 23% were females with male to female ratio of 2.9:1 (Graph 1). The mean age was 62.45 ± 8.18 years and median age was 62 years and ranged between 40 to 93 years. Most of the patients (43.7%) were aged between 61 to 70 years (Graph 2). Overall 51.37% of the patients had positive history of hypertensive treatment, followed by history of diabetes mellitus, prior revascularization, smoking, CCF and CKD. None of the patient had heterozygous familial hypercholesterolemia (Graph 3).



Graph 1: Distribution of patients according to the sex.



Graph 2: Distribution of patients according to the age.



Graph 3: Distribution of patients according to the risk factors.

With regarding to lipid abnormalities, majority of the patients (60.61%) had low HDL followed by hypertriglyceridemia, elevated LDL and hypercholesterolemia. The mean HDL, triglycerides, LDL and total cholesterol levels were noted as 38.90 ± 13.44 mg/dL, 89.97 ± 43.09 mg/dL, 145.73 ± 85.23 mg/dL and 156.98 ± 49.52 mg/dL respectively (Table 1).

Parameters	Mean (n=952)		Median	Range	
	Mean	SD		Min	Max
Total cholesterol (mg/dL)	156.98	49.52	152	42	651
HDL cholesterol (mg/dL)	38.9	13.44	37	12	151
LDL cholesterol (mg/dL)	89.97	43.09	86	11	486
Triglycerides (mg/dL)	145.73	85.23	127	25	797

Table 1: Clinical profile of the patients.

The very high risk and stable ASCVD (high risk) was noted in 494 (51.89%) and 458 (48.11%) patients respectively. In those with very high risk of ASCVD again males outnumbered females with male to female ratio of 3.7:1. Most of the patients (39.08%) with high risk of ASCVD belonged to sixth decade of life but, 49.39% of the patients with very high risk ASCVD were aged between 61 to 70 years. In 494 patients with very high risk of ASCVD, 60.73% of the patients had positive history of hypertensive treatment and most of the patients (56.48%) had low HDL (Tables 2 and 3). In 458 patients with stable ASCVD (high risk), 41.27% of the patients had positive history of hypertensive treatment and most of the patients (65.07%) had low

HDL. The other risk factors and lipid abnormalities are as depicted in Tables 2 and 3.

Risk factors	ASCVD			
	ASCVD high (n=458)		ASCVD very high (n=494)	
	No.	%	No.	%
Positive history of hypertensive treatment	189	41.27	300	60.73
History of diabetes mellitus	162	35.37	285	57.69
History of prior revascularization	79	17.25	224	45.34
History of smoking	80	17.47	102	20.65
History of congestive heart failure	40	8.73	66	13.36
CKD (eGFR 15-59 mL in/1.73)	4	0.87	20	4.05
Heterozygous familial hypercholesterolemia	0	0	0	0

Table 2: Distribution of patients according to the ASCVD risk factors.

Discussion

In this study males outnumbered females with a male to female ratio of 3.3:1 in other words there is three-fold risk of ASCVD in males compared to females and suggests that male sex is a strong risk factor for ASCVD. Furthermore, males outnumbered females in patients with

high risk (2.9:1) and very high risk of ASCVD (3.7:1) was noted. This observation is consistent with the MASALA study [13] (Mediators of Atherosclerosis in South Asians Living in America) which predicted male sex as a strong risk factor for coronary artery calcification (CAC). Also, the NYC CHS (New York City Community Health Survey) a small cohort of South Asians [14] with hypertension (n=144) compared with Chinese (n=555) and NHWs (n=5987), and in this study, the South Asians with hypertension were more likely to be males. In a very recent study by Hassana et al. [15] from Pakistan, Males (4.09; 95% CI=3.4–4.93) had high odd ratios in ≥ 20 ASCVD risk score. Hence together with other studies it is evident that, male sex is at high risk of developing ASCVD compared to females.

Lipid profile	ASCVD				Total (n=952)	
	ASCVD high (n=458)		ASCVD very high (n=494)			
	No.	%	No.	%	No.	%
Hyper-cholesterolaemia (≥ 200 mg/dL)	79	17.25	91	18.42	170	17.86
Low HDL (<40 mg/dL)	298	65.07	279	56.48	577	60.61
Elevated LDL (≥ 100 mg/dL)	171	37.34	190	38.46	361	37.92
Hyper-triglyceridaemia (≥ 130 mg/dL)	231	50.44	232	46.96	463	48.63

Table 3: Distribution of patients according to the ASCVD risk factors with respect to lipid profile.

In this study overall, age ranged between 40 to 93 years and the mean age was 62.45 ± 8.18 years and median age was 62 years. Most of the patients (43.7%) were aged between 61 to 70 years. However, patients with high risk were slightly younger that is, 39.08% of the patients belonged to sixth decade but most of the patients with very high risk ASCVD (49.39%) were aged between 61 to 70 years suggesting that, the frequency of ASCVD peaked during sixth and seventh decade of life. This observation was consistent with the finding of a study Hatawalkar et al. [16] in which among other cohorts of 4 ethnicities (NHWs, Asians, Hispanics, and blacks), Asian Indians were investigated for coronary artery calcification (CAC) burden compared with the other racial/ethnic groups. Asian Indians, who represented approximately 10% of the cohort, had an increased mean calcium score, and the Asian Indian race was a significant independent predictor of CAC severity, even when controlling for traditional ASCVD risk factors. Among those >60 years of age, the prevalence of high CAC burden (scores >100) in Asian Indians is greater than in all other ethnic groups. In a very recent study by Hassana et al. [15] overall low risk score <7.5 was observed in <50 years age group and high-risk score ≥ 7.5 was observed in ≥ 50 years age group. Also, the odds ratios of subjects of age ≥ 50 years had 9.73 (95% CI=7.24–13.06) times higher risk of ASCVD.

In the present study the common risk factor noted was positive history of hypertensive treatment (60.73%) followed by diabetes mellitus (57.69%), history of prior revascularization (45.34%), smoking (20.65%), CCF (13.36%), and CKD (4.05%). None of the patients had heterozygous familial hypercholesterolemia. Hypertension is an important risk factor for the development of CVD. In native South Asians, there is an increased risk of AMI in those with a history of hypertension and urbanization has had a negative impact on CVD risk

factors. Reports have also shown worse coronary risk factors, including hypertension, in South Asians who migrate to the United Kingdom or Canada compared with native South Asians [17]. In the United States, one of the most common CVD risk factors in South Asians is hypertension, with a prevalence of 43% in men and 35% in women in the MASALA study [18] and an overall age-adjusted prevalence of 27% as shown in the NYC CHS (New York City Community Health Survey) [14].

Pertaining to lipid abnormalities, low HDL was widely prevalent (60.61%) followed by hypertriglyceridemia (48.63%), Elevated LDL (37.92%) and Hypercholesterolemia (17.86%). Dyslipidemia is likely an important factor contributing to the increased CVD risk observed in South Asian populations. The typical lipoprotein pattern seen in individuals of South Asian descent who are living in Western societies is characterized by hypertriglyceridemia and low levels of HDL cholesterol (HDL-C). Although levels of low-density lipoprotein (LDL) cholesterol (LDL-C) may not appear elevated, this population has a high incidence of qualitatively abnormal LDL-C particles characterized by smaller size and lower density. In a study that compared South Asian individuals living in India with those living in the United States, potential pathophysiological explanations for the atherogenic dyslipidemia pattern include a higher prevalence of insulin resistance, which is frequently seen in South Asian populations, and abnormalities in CETP (cholesteryl ester transfer protein). South Asian populations have been found to have 30% higher CETP activity levels than comparable European populations after adjustment for age, sex, BMI, and waist circumference ($p < 0.0001$). This was positively associated with higher triglycerides and increased LDL-C particle number and inversely associated with HDL-C and LDL-C particle size [19]. A study of $>16,000$ Asian Indians in California by Frank et al. [20] showed that Asian Indians were 3 times more likely to have low HDL-C (odds ratio [OR], 3.93 for women and 3.00 for men; $p < 0.001$) and twice as likely to have high triglycerides (OR, 2.12 for women and 2.67 for men; $p < 0.001$) compared with NHWs and only slightly more likely to have high LDL-C (OR, 1.16 for women and 1.30 for men; $p < 0.001$). Small, dense LDL-C particles are known to be associated with increased triglyceride and apolipoprotein B levels, and the INTERHEART study showed elevated apolipoprotein among South Asians with MI compared with subjects from other countries (61.5% versus 48.3%, respectively) [17].

The first report with large and appropriate sample size detailing the risk of ASCVD from Pakistan by Hassana et al. [15] highlighting that history of current smoking, high cholesterol, type 2 diabetes and hypertension are considered as a major potential underlying risk factor for ASCVD. Other than these risk factors, the present study adds history of prior revascularization, history of CCF and CKD as additional risks factors though in smaller proportion but cannot be neglected which are also focused on ACC/AHA calculator. However, these additional risk factors require further validation due to relatively smaller sample size and lack of nationally representative data.

Conclusion

Most common risk factor for ASCVD is hypertension followed by diabetes, dyslipidemia and smoking. With incidence being higher in very high clinical ASCVD compared to stable ASCVD. The present study adds history of prior revascularization, history of CCF and CKD as additional risks factors though in smaller proportion but cannot be neglected which are also focused on ACC/AHA calculator. Male sex is at high risk of developing ASCVD compared to females.

Conflicts of Interest

There are no conflicts of interest for the present study.

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