Predicting the risk of atherosclerotic cardiovascular disease (ASCVD) in Pakistani population

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A R T I C L E   I N F O

A B S T R A C T

Objective: To assess the risk of developing atherosclerotic cardiovascular disease (ASCVD) in Pakistani population.

Methodology: This cross-sectional study includes 9885 subjects with ASCVD risk. Baseline demographic characteristics were obtained by using predesigned questionnaire. Clinical tests were analyzed by collecting fasting blood sample. Risk calculator application (Software) developed by ACC/AHA used to score the risk of ASCVD. Risk score with age group < 7.5 was considered low at risk and ≥7.5 high at risk.

Results: Mean age of subjects was 49.42 ± 10.58 years. Significant difference for basic demographic and clinical characteristics ($p < 0.0001$) was observed except for diabetes and hypertension. Subjects of age ≥50 years had 9.73 (95% CI = 7.24–13.06) times higher risk of ASCVD in ASCVD risk score15–19.9. Males 4.09 (95% CI = 3.4–4.93) times, subjects with diabetes 5.8(95% CI = 4.86–6.93) times and smokers 2.05(95% CI = 1.68–2.49) times had greater chance of ASCVD in ≥20 risk score respectively. Subjects with high cholesterol and taking treatment for hypertension had greater chance of ASCVD in ≥20 ASCVD risk score, while significantly high odd ratio in all ASCVD risk score was observed for Systolic Blood Pressure.

Conclusion: Our findings are comparable as per the reported international data highlighting that history of current smoking, high cholesterol, type 2 diabetes and hypertension are considered as a major potential underlying risk factors for ASCVD in Pakistani individuals.

1. Introduction

Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of death and disability worldwide, which may present as coronary heart disease, stroke, and peripheral arterial disease.[1,2]

The prevalence of modifiable and non-modifiable risk factors for atherosclerosis are alarmingly high in the Pakistani population as the rates of other related cardiovascular disorders vary greatly between groups of population.[3] Previous data suggested that in the time period of 10 years 82.15% of the target Pakistani population had a low risk of atherosclerosis while 17.85% had high risk. Furthermore, in the life span of the target population, 78.03% had high risk of atherosclerosis while 21.97% had low risk.[3]

A substantial portion of the ASCVD resulting from obesity is also mediated by type 2 diabetes with several other risk factors that are unknown.[4] Major risk factors for ASCVD are hypercholesterolemia, hypertension, hyperglycemia and emerging risk factors that include atherogenic dyslipidemia, insulin resistance, pro-inflammatory state and pro-thrombotic state.[5] Numerous risk scores have also been developed to predict ASCVD risk.[6] Till date various physiological biomarkers based on serum lipid, glucose and hormone biomarkers serum lipid, glucose and hormone profile have been identified that are related to increased ASCVD risks.[7] Prevention plays major role to reduce the adverse consequences of risk factors for ASCVD.[8]

The American College of Cardiology (ACC) and the American Heart Association (AHA) have recently developed new standards for handling

Table 1
Clinical Characteristics of the study participants.

Parameter	Male n (%)	Female n (%)	P-value	Overall n (%)
n	5010 (50.6%)	4875 (49.3%)		9885
Age (years) [*]	50.66 ± 10.71	48.14 ± 10.30	< 0.0001	49.42 ± 10.58
Diabetes [α]	2191 (44.1%)	2162 (44.8%)	0.516	4353 (44.5%)
Current Smoking [α]	1533 (31.3%)	90 (1.9%)	< 0.0001	1623 (17.0%)
Systolic blood pressure [α]	130.88 ± 21.12	132.77 ± 21.5	< 0.0001	131.8 ± 21.33
HTN treatment [α]	2428 (49.7%)	2390 (50.0%)	0.717	4818 (49.9%)
Cholesterol Status [α]				
Desirable	3416 (69.9%)	3152 (65.7%)	< 0.0001	6568 (67.8%)
Moderate	1145 (23.4%)	1226 (25.6%)		2371 (24.5%)
High	327 (6.7%)	417 (8.7%)		744 (7.7%)
Recommendation [α]				
Moderate intensity statin (MIS)	1935 (39.1%)	1990 (41.1%)	< 0.0001	3925 (40.1%)
High intensity statin (HIS)	1274 (25.7%)	594 (12.3%)		1868 (19.1%)
Life style modifications (LSM)	809 (16.3%)	1232 (25.4%)		2041 (20.8%)
No recommendation	933 (18.8%)	1025 (21.2%)		1958 (20.0%)
Risk Score [α]				
Less than 7.5	3032 (60.5%)	3815 (78.3%)	< 0.0001	6847 (69.3%)
7.5–9.9	409 (8.2%)	369 (7.6%)		778 (7.9%)
10–14.9	577 (11.5%)	303 (6.2%)		880 (8.9%)
15–19.9	283 (5.6%)	128 (2.6%)		411 (4.2%)
greater than 20	709 (14.2%)	260 (5.3%)		969 (9.8%)

Data presented as Mean ± SD or n (%).

P-value < 0.05 was considered statistically significant.

[*] use Independent *t*-test.

[α] Chi-square test.

blood cholesterol.[9] The new guidelines mention initiation of healthy lifestyle modifications and 3-hydroxy-3-methylglutaryl coenzyme-A reductase inhibitor ("statin") treatment in subjects with a great risk for atherosclerotic cardiovascular disease.[10] The eventual goal of the new cholesterol guidelines is to diminish a person's risk of heart attack, stroke and death. For this reason, the measuring and treating cholesterol is not just on consideration, but finding whether someone previously has or is at risk for atherosclerotic cardiovascular disease (ASCVD) and could benefit from treatment. If a medication is needed, statins are recommended as the first choice to reduce heart attack and stroke among certain higher-risk patients based on an overwhelming quantity of evidence. For subject's incapables to take a statin, many other cholesterol-lowering drugs are available; however, there are few research to support their use.[11]

The aim of the current study was to estimate the ASCVD risk in Pakistani population with potential major risk factors which includes diabetes, hypertension and hypercholesterolemia.

2. Methodology

This cross-sectional study was conducted at multiple primary and secondary care centers of Pakistan. The subject recruitment period was from June 2016 to December 2016. Team was assigned the task to enroll subjects for the study after obtaining informed consent.

Data was obtained from 192 clinics of all over Pakistan, from each community including both rural and urban areas. Total of 9885 subjects with age < 40 years up to 79 years were recruited. Subjects suffering from hypertension, hypercholesterolemia, atherosclerotic cardiovascular disease (ASCVD) and having current smoking habit (20 cigarettes per day) and medications especially antihypertensive were included in the study. Also, both known diabetic subjects and subjects having no diabetes are also included in the study. ASCVD risk was considered as the risk of developing the first ASCVD event over a 10-year period among population without ASCVD at baseline. According to ACC/AHA calculator active heart disease subjects or subjects having prior heart attack and stroke were excluded from the study.

Basic demographic characteristics of the study subjects such as age,

gender, current smoking, diabetes and systolic blood pressure were collected on a predesigned questionnaire. Current cigarette smoking was self-reported by participants. For every screened patient, which had the treatment recommendations by the Blood Cholesterol Guidelines of ACC/AHA that addresses the use of fixed doses of cholesterol-lowering drugs (statins) to reduce the risk of ASCVD were also noted.[12] Statin therapies used in the study were moderate intensity statin (MIS), high intensity statin (HIS) and life style modifications (LSM).

Estimation of glucose was done by using Glucometer (AccuChek, Roche). Systolic and diastolic blood pressure were measured using mercury sphygmomanometer after five minutes of rest in sitting position of patients. Hypertension was divided into following categories: normal (< 120/80), prehypertension (120–139/80–89), stage 1 hypertension (140–159/90–99) and stage 2 hypertension (> 160/100).[13,14] Total cholesterol level was estimated with CHOD-PAP (Cholesterol oxidase) enzymatic colorimetric method and categorized into desirable, moderate and high as < 200, 200–239 and > 240 respectively.[15] The collected data was used to score the risk according to subjects age group < 50 years and ≥50 years age groups. By using an ASCVD risk calculator application (Software) developed by ACC/AHA risk scores with age groups were categorized into < 7.5, 7.5–9.9, 10-14.9, 15-19.9, > 20.[16,17]

Data was analyzed on Statistical Package for Social Sciences (SPSS) version 20. Data was presented as Mean ± S.D for continuous variables and frequency with percentage for categorical variables. *T*-test and Chi square test was used. A multinomial logistic regression analysis was conducted to determine the risk factors of ASCVD. P-value < 0.05 was considered statistically significant.

3. Results

A total of 9885 subjects consisting of 5010 males and 4875 females were included in the current study. The mean age of subjects was 49.42 ± 10.58 years. Percentage of male smokers was significantly higher (p < 0.0001) as compared to females. Out of 9885 subjects, 4353 (44.5%) had diabetes. Total cholesterol was estimated as desirable, moderate and high in 6568 (67.8%), 2371 (24.5%) and 744

Table 2
Multinomial logistics regression analysis of demographic clinical parameters of study participants.

Parameters	ASCVD Score Status			
	7.5–9.9	10–14.9	15–19.9	≥20
Age ≥50 years*	3.76 (3.15–4.48)	5.36 (4.48–6.41)	9.73 (7.24–13.06)	4.06 (3.44–4.8)
Gender (Male)*	1.59 (1.32–1.91)	2.81 (2.35–3.37)	3.41 (2.65–4.39)	4.09 (3.4–4.93)
Diabetes*	2.03 (1.72–2.41)	2.19 (1.86–2.58)	3.27 (2.59–4.13)	5.8 (4.86–6.93)
Smoking*	1.63 (1.3–2.04)	1.51 (1.22–1.86)	1.51 (1.14–2)	2.05 (1.68–2.49)
High Cholesterol*	1.52(1.27–1.81)	1.84 (1.55–2.18)	2.11(1.68–2.66)	3.53 (3–4.15)
Systolic Blood Pressure ≥120 mg/dl*	2.07 (1.71–2.51)	2.29 (1.9–2.77)	2.7 (2.05–3.54)	1.78 (1.49-2.12)
HTN treatment*	1.67 (1.4–1.99)	1.5 (1.27–1.78)	1.32 (1.05–1.67)	2.01 (1.69–2.39)

Reference category is: ASCVD score < 7.5.
Data presented as OR (95% Confidence interval).
 * statistically significant at P-value < 0.001.

(7.7%) subjects respectively. Subjects on cholesterol treatment of MIS and HIS were 3925 (50.1%) and 1868(23.8%) respectively. LSM in 2041(20.8%) subjects and no recommendation in 1958(20.0%) subjects were observed. Around 49.9% of this study subjects were using anti-hypertensive drugs. Total risk score (ASCVD) was calculated as less than 7.5 in 6847(69.3%), 7.5–9.9 in 778(7.9%), 10–14.9 in 880(8.9%), 15–19.9 in 411(4.2%) and greater than 20 in 969(9.8%) of the subjects. Significant difference was observed in all variables (p < 0.0001) except for diabetes and hypertension (Table 1).

From multinomial logistics regression (Table 2), the odds ratios of subjects of age ≥50 years had 9.73 (95% CI = 7.24–13.06) times higher risk of ASCVD observed in 15–19.9 ASCVD risk score. Males 4.09 (95% CI = 3.4–4.93) had high odd ratios in ≥20 ASCVD risk score. Similarly, people with diabetes 5.8(95% CI = 4.86-6.93) times and smokers 2.05(95% CI = 1.68–2.49) times greater chance of ASCVD in ≥20 risk score. Subjects with high cholesterol and taking treatment for hypertension had also greater chance of ASCVD in ≥20 ASCVD risk score, while significantly high odd ratio in all ASCVD risk score was observed for Systolic Blood Pressure.

Table 3 compare the risk score of ASCVD with age groups. Low risk score < 7.5 was observed 3874(64.3%) in < 50 years age group and this percentage was decreased in ≥50 years age group. Similarly, < 50 years vs ≥50 years age groups [247(31.3%) vs 543(68.7%)] in 7.5-9.9% risk score, [210(23.7%) vs 676(76.3%)] in 10–14.9% risk score, [62(14.9%) vs 353(85.1%)] in 15–19.9 risk score and [291(29.7%) vs 689(70.3%)] in ≥20 risk score shows high risk in ≥50 years age groups. Statistically significant (p < 0.0001) results were found in all age groups.

4. Discussion

Atherosclerotic cardiovascular disease (ASCVD) and cardiovascular heart disease (CHD) have declined in the world in the past two decades, likely due to improvements in blood pressure, cholesterol control and decline in smoking.[18] In this study, 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. Previous study shows that Urdu speaking Pakistanis were at higher risk of ASCVD.[19] Ethnicity was

beyond from this study. The prevalence of ASCVD and major risk factors as undesirable cholesterol, systolic blood pressure, diabetes and history of smoking were also calculated to be significantly higher in subjects in the current study.

Although several other major risk factors for ASCVD also exists. Elevated low-density lipoprotein (LDL) cholesterol and a low level of plasma high density lipoprotein (HDL) cholesterol are a strong and independent risk factors for ASCVD for the past 2 decades, lowering of LDL levels and improving HDL levels will reduce risk for ASCVD.[20,21] We focused on ACC/AHA calculator referring to total cholesterol and HDL only. Data collection of multiple parameters for convenience sampling from 192 clinics of each community including both from rural and urban areas across Pakistan within a short time period is a strength of this study.

Previously, both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were inversely associated with overall mortality, but no significant interactions were found for DBP with prevalent ASCVD.[22] This signifies the reason of using SBP as a marker to diagnose hypertension. Many subjects without history of hypertension had high blood pressure and a large number of participants already on anti-hypertensives also had elevated blood pressure pointing towards inadequate control and results in high risk of ASCVD. It is reported as an important and alarming situation at national level. Elevated serum cholesterol was reported as a major risk factor for ASCVD. Previously, it was studied that this elevation signifies an increase in apolipoprotein B (apo. B)-containing lipoproteins.[23] Levels of serum cholesterol vary widely throughout the world, glycemic control is also considered beneficial for modifying plasma lipid levels, particularly in subjects with high cholesterol and poor glycemic control.[24,25]

The majority of high-risk patients of ASCVD require drug therapy, usually statins are recommended by the ACC/AHA guidelines as preventive measures in elder patients with favorable risk factors, regardless of sex and ethnicity.[26] It was previously noted that significant heterogeneity exists among those who were eligible for statins. High-intensity statin ≥7.5 risk score and moderate intensity statin < 7.5 risk score therapy with lifestyle modification were recommended for subjects with diabetes and ASCVD after clinician-patient discussion.[27] Lifestyle changes are essential and recommended before and during the

Table 3
Risk Score of ASCVD with age group of the participants with major risk factors.

Age Status	Score Status					P-value
	< 7.5	7.5–9.9	10–14.9	15–19.9	≥20	
< 50	3874 (64.3%)	247 (31.3%)	210 (23.7%)	62 (14.9%)	291 (29.7%)	< 0.0001
≥50	2149 (35.7%)	543 (68.7%)	676 (76.3%)	353 (85.1%)	689 (70.3%)	

Data presented as n (%).
Chi-Square test was used.
P-value < 0.05 was considered statistically significant.

use of cholesterol lowering drug therapies. These changes are crucial components of health promotion and ASCVD risk reduction in both primary and secondary prevention. Major interventions of the current study included smoking cessation, dietary changes, medical nutrition therapy, weight loss (if overweight), and exercise which aids in reducing ASCVD risk factors among participants.

Convenience sampling was used for data collection is the limitation of our study. Unfortunately, there is insufficient data to reliably predict risk for those < 40 years of age and for those with total cholesterol > 320 mg/dl using this ACC/AHA risk calculator, therefore, we did not include data of subjects having cholesterol > 320 mg/dl but few subjects having less than 40 years of age were included which lack evidence in our study. Only known ASCVD subjects from concerned hospital are included and investigations like angiography, coronary artery calcification, intimal thickness are beyond the scope of this study. We focused on ACC/AHA calculator using total cholesterol and HDL only. So, results calculated for ASCVD are not based on LDL and VLDL. However, with scarce reported data on risk of ASCVD from the region, the reports from this study may still be worthwhile to conduct well planned future studies accounting all these shortfalls.

5. Conclusion

To the best of our knowledge, this is the first report with large and appropriate sample size detailing the risk of ASCVD. Our findings are comparable as per the reported international data highlighting that history of current smoking, high cholesterol, type 2 diabetes and hypertension are considered as a major potential underlying risk factors for ASCVD in Pakistani individuals.

Author contributions

K Hassan: Concept and design, reviewed and revised the manuscript.

B S Mohydin: Concept and design, reviewed and revised the manuscript.

A Fawwad: undertook the data analyses, reviewed and revised the manuscript.

N Waris: Interpretation of data, wrote and reviewed the manuscript.

S Jafri: Data collection and Interpretation of data.

M Jawaid: Reviewed and revised the manuscript.

Conflict of interest

There is no conflict of interest regarding the publication of this article.

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