Need of statins among un-diagnosed unaware Pakistanis via revised pool cohort equation by American Heart Association

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Abstract: National diseases burden of cardiovascular diseases is the top leading cause of death in Pakistan. In this study, Pakistani has been assessed for Atherosclerotic Cardiovascular Disease (ASCVD) on the basis of American Herat Association (AHA) guidelines. The aim of the study is to assess and inform about 10-year risk and life time risk in people residing in the largest metropolis city Karachi and aware about the use of statins as per revised Pooled Cohort Equation guidelines. The study sample size was 1760 with the age of 39 to >80 years with non-atherosclerotic diseases. Both genders without language barrier with or without elevated lipid were included. Clinical investigations including HDL, B.P and serum TG were included for calculating the ten year and life time risks on the basis of <5%, 5-7% and >7.5%. Results shows that the Odd ratio >1 found between age and TC however significant relationship ($p<0.05$) between gender, diabetes, hypertension and smokers were established. >50% study population required moderate and high intensity statin however <30% needed life style modification for reducing cardiac on risk. It is concluded that current recommendations are not for South Asians and may under or overlook the risks of individuals living in this continent. This study estimates the cardiovascular risk burden in the population of Karachi, Pakistan who were non-atherosclerotic undiagnosed and un-treated. This risk assessment may modify the algorithm and successfully identify the risk burden in present study groups.

Keywords: Statins, ASCVD risk, pooled cohort equation, Karachi.

INTRODUCTION

Every year more than 15 million mortalities occur in the world caused by cardiovascular diseases. More than 15 million death count was recorded worldwide in the year 2010 due to CVDs. People who die of cardiovascular diseases are aged below 65 which is considered as a premature age given the today's increased span of life. The increased death incidences of cardiovascular diseases have placed socio-economic burden on people belonging from the developing countries (Iqbal *et al.,* 2004, Nichols *et al.*, 2014). The causes that trigger cardiovascular diseases include tobacco consumption, hypertension, poor diet and lifestyle, obesity and lack of exercise (Omran, 2005). The CVDs tend to afflict people in their peak working years hence even after being diagnosed or at the risk of CVDs; no proper medical approach is made by the sufferers due to less cost effective therapeutic strategies (Gaziano, 2007).South Asians (ancestors from Pakistan, Bangladesh, India, Sri Lanka and Nepal) have relatively high risk of CVD as compared to other regions and specifically it is higher in young people (Forouhi and Sattar, 2006)

Pakistan is one of the South Asian countries which present a large number of death incidences due to cardiovascular disorders. According to World health organization (WHO), globally 30% fatalities are reported due to CVDs (Organization, 2015). The risks of cardiovascular diseases are equally prevalent in both urban and rural areas of Pakistan (Nuri *et al*., 2012). Prevention requires immense work to reduce the adverse outcomes of risk factors for cardiovascular disease (Nuri *et al*., 2012). For minimizing the cardiovascular risk, the American heart association in 2013 introduced the pooled cohort equation for estimating 10 years risk and life time risk. The 10 year risk was evaluation by Atherosclerotic Cardiovascular Disease (ASCVD) event which is non-fatal CHD or MI, a non-fatal or fatal stroke over a 10 year period in people who did not have ASCVD initially i.e., at the beginning of 10 years (Goff *et al*., 2014, Bennett *et al*., 2013). A study conducted was limited to participants of two specific part of USA to evaluate the association of lifetime and 10-year risk of CVD with sub-clinical atherosclerosis in south Asians which does not present true south Asians in these regions (Bhopal *et al*., 2005). Another study validated the pool cohort equation/ calculator and give good calibration results in Asian population (Chia *et al.*, 2014).

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The objective of our study is to assess and inform about 10-year risk and life time risk in people residing in the largest metropolis city Karachi, Pakistan and determine the need of statins and life style modification as per revised Pooled Cohort Equation (RPCE) 2018.

MATERIALS AND METHODS

For our study, the people living in Karachi from different ethnic backgrounds have volunteered who happened to be the attendants of patients from 2 tertiary care hospital of Karachi. External Institutional review board (IRB) approval has been taken from Jinnah University for Women. The study population who were unaware and undiagnosed having age between 39 to >80 was selected. The study participants were 2093 who were requested to carry out the clinical tests i.e. total cholesterol (mg/dl), HDL Cholesterol (mg/dl) and Systolic BP (mm/Hg) (Yadlowsky *et al*., 2018). However, 1760 were re-visited with clinical test and further follow up. Inclusion criteria for the questionnaire was gender of both sexes, presence or absence of diabetes, presence or absence of hypertension and its treatment and presence or absence of smoking by the participants. The participants had given consent and were expected to visit for follow up. The questionnaire was translated into different languages for better understanding of the participants. We concluded participants with hypertension when the systolic blood pressure is ≥140 mm Hg. We stated dyslipidemia when total cholesterol is ≥240 mg/dl, HDL levels <40mg/dl and triglyceride levels between 151.1-203.1 mg/dl(Kandula *et al*., 2014).We examined blood pressure using automated B.P monitor for three times and mean value was taken. For lipid profile, blood samples were collected post 12 hours of fasting and examined total cholesterol (mg/dl), serum triglyceride (mg/dl) and HDL (mg/dl) determined by using standard methods. All test data were put into the calculator or pooled cohort equation and it automatically calculated the 10 year and life time risk of the participants with recommendation of Moderate, High intensity statins and life style modifications.

RESULTS

The total study participants were 1760 (Male 42.7%, Female 57%). Age was stratified in different groups in which 40-49 years were the highest risk (32.9%). The pooled cohort equation has attributed > 40 years old individuals for the purposes of 10-year risk assessment and life time risk; however, this risk assessment may be less accurate or underestimated (Preiss and Kristensen, 2015). It was also concluded that the patients having elevated risk ≥ 7.5% have proposed to replace the Framingham Risk 10-year CVD calculation, which was recommended for use in the NCEP ATP III guidelines for high blood cholesterol in adults (Cleeman *et al*., 2001). By using descriptive statistics, Patient demographics were given in table 1 in which known diabetes cases were 49.5%, hypertensive were 46.5% and smoker were 18%.

The calculated risk factor for undiagnosed unaware study sample were bifurcated into 5 groups i.e. <7.5, 7.5-9.9, 10-14.9, 15-19.9 and >20 as per AHA guidelines. We observed that highest risk factor (>20) was observed

Table 1: Demographics and risk indicators as per revised pooled cohort equation

Groups	Range	N (%)
Age	31 - 39 years	(370) 21.02 %
	40 - 49 years	(579) 32.9%
	50 - 59 years	(515) 29.3%
	60 - 69 years	(228) 13.0%
	70 - 79 years	(62) 3.5%
	>= 80 years	(6) .3%
Gender	Male	(753) 42.7%
	Female	(1007) 57%
Diabetes	Yes	(872) 49.5%
	No	(888) 50.4 %
Hypertension	Yes	(819) 46.5%
	No	(734) 41.7%
	Don't know	(207) 11.7%
Smoking	Yes	(322) 18%
	No	(1438) 81%
Family history of premature CVD	(592) 35%	
BMI	29.81±4.6	
Heart rate (beats/min)	89 ± 17	
Systolic blood pressure (mmHg)	117.2 ± 20.7	
Diastolic blood pressure (mmHg)	69.7 ± 13.7	

Table 2: Contributing Risk Factors for Coronary Heart Disease among Pakistani Adults without Self-Reported Coronary Heart Disease

		Score Risk					
		7.5-9.9	10-14.9	15-19.9	>20	<7.5	P value
		(N) %	(N) %	(N)%	(N) %	(N) %	
Gender	Male	(90) 44%	(108) 56%	(97) 70%	(135) 67.9%	(308) 30.0%	0.00
	Female	(112) 55%	(85) 44%	(41) 30%	(64) 32.1%	(720) 70.0%	
Ethnicity	Punjabi	(99) 40%	(109) 43%	(68) 40%	(114) 47%	(493) 58%	0.17
	Urdu	(89)36%	(80) 32%	(40)23%	(67) 27%	(178) 21%	
	Sindhi	(45) 18%	(38)15%	(40) 23%	(45)18%	(118)14%	
	Pathan	(12)5%	(26) 10%	(24)14%	(19) 8%	(56) 7%	
Diabetes	Yes	(98) 65%	(122) 61%	(98) 69.3%	(235) 82%	(449) 45.7%	0.00
	No	(52) 35%	(78) 39%	(44) 30.7%	(50) 18%	(534) 54.3%	
HTN	Yes	(123) 66%	(108)58%	(123) 75%	(142) 62%	(457) 45.9%	0.00
	No	(62) 34%	(78) 42%	(41) 25%	(88) 38%	(538) 54.1%	
Smoker	Yes	(60) 34%	(67) 33%	(45) 37%	(84) 31%	(112) 11%	0.00
	No	(114) 66%	(134) 67%	(76) 63%	(190) 69%	(878) 89%	

Table 3: Contributing risk factors of ASCVD among unware un-diagnosed study population

N=1760		Score Risk					P-Value
		7.5-9.9	10-14.9	15-19.9	>20	<7.5	
		N (%)	N (%)	N (%)	N (%)	N(%)	
Age	<39	10(5.1%)	4 (1.9%)	0 (0%)	7(4.9%)	166(15.6 %)	0.000
	40-49	50 (25.4%)	43 (20.6 %)	12 (8 %)	11 (7.7 %)	496 (47.7 %)	
	50-59	90 (45.7 %)	79 (37.8 %)	80 (53.3 %)	40 (28.2 %)	315 (29.6 %)	
	60-69	43 (21.8 %)	70 (33.5 %)	49 (32.6%)	47 (33.0 %)	69 (6.5 %)	
	70-79	4 (2%)	13(6.2%)	9 (6.2 %)	34 (24.0 %)	10 (1%)	
	>80	0 (0%)	0 (0%)	0 (0%)	3 (2.1%)	3 (0.3%)	
TC	<200	(78) 45.9%	(101) 50.5%	(70) 56.8%	(92) 53.4%	(712) 65.9%	0.000
	200-239	(61) 35.9%	(60) 30.0%	(40) 30.5%	(50) 27.9%	(274) 25.4%	
	>240	(31) 18.2.7%	(39) 19.5%	(21) 16.0%	(37) 20.7%	(94) 8.7%	
SBP	<120	(47) 25.0%	(57) 28.0%	(31) 26%	(34) 19%	(450) 42%	0.000
	120-139	(42) 22.0%	(40) 19.0%	(14) 12.0%	(43) 24%	(233) 22%	
	140-159	(53) 28.0%	(69) 33.0%	(51) 43%	(57) 32%	(246) 23%	
	>160	(46) 24.0%	(41) 20.0%	(23) 19%	(43) 24%	(140) 13%	
DBP	<80	(49) 32.0%	(63) 50%	(52) 38%	(86) 34%	(438) 40%	0.310
	80-89	(13) 9.0%	(19) 15%	(17) 13%	(37) 15%	(243) 22%	
	90-99	(45) 30.0%	(26) 21%	(52) 38%	(113) 45%	(246) 22%	
	>100	(44) 29.0%	(18) 14 %	(15) 11%	(17) 7%	(167) 15.0%	

among the age group of 40 to < 80 years and significant relationship were observed with gender, diabetes, hypertension and smoker (p<0.005). As per AHA guidelines >5% risk required life style modification.

By using Pearson chi square, the significant relationship was found in between the contributing risk factors including gender (p=<0.005), diabetes (p=<0.005), hypertension and smokers (p=<0.005) as shown in table 2. However, no significant relationship was observed between ethnic groups (p=0.17).

Chi-squared goodness-of-fit test applied for evaluating the significance relationship between score risk and Age, Total cholesterol and Systolic Blood pressure (p<0.005) as shown in table 3.

For determining the strength of association odd ratio (OD) were calculated between Age and total cholesterol as it shows significant relationship. The OD greater than 1 found is all risk groups with TC as shown in table 4 which indicates higher odd of outcomes in individuals.

The study population's results concluded by AHA RPCE that all groups need to consider statins excluded <7.5 %. High intensity statins (HIS) and Moderate intensity statins (MIS) need to recommend more than 90% of study population however minimum populations need Life style

Table 4: Odd ratio association with Age and TC group

AHA Score Risk		Sig.	ODD Ratio	95% Confidence Interval for	
				Lower Bound	Upper Bound
Age with Total Cholesterol (TC)					
10-14.9		.003	1.040	1.013	1.067
15-19.9		.000	1.070	1.036	1.106
>20		.000	1.121	1.089	1.155
<7.5		.000	.908	.888	.927
Total Cholesterol (TC)					
10-14.9	TC Groups				
	< 200	.239	1.431	.788	2.596
	200-239	.886	1.048	.553	1.986
	>240	-	-	-	-
15-19.9					
	< 200	.168	1.741	.791	3.828
	200-239	.733	1.160	.493	2.729
	>240	-	-	-	-
>20					
	< 200	.532	1.216	.658	2.245
	200-239	.591	.833	.427	1.623
	>240	-	-	-	-
<7.5					
	< 200	.000	4.041	2.481	6.584
	200-239	.005	2.086	1.245	3.495
	>240	-	-	-	-

Table 5: Requirement of statins as per AHA guidelines

Risk Score	HIS MIS	LSM & no recommendation	Total	P Value
7.5-9.9	182	-	183	0.00
10-14.9	201	-	202	
15-19.9	89	-	90	
>20	153	-	163	
<7.5	653	469	1122	
Total	1278	469	1760	

modification (LSM) i.e. <7.5% risk score along with no statins recommendations as given in table 5.

DISCUSSION

The American college of cardiology and heart association released a calculator to determine the 10 years and life time risk of individuals(Stone *et al*., 2014). This equation based on four different populations of American by using cohort studies (Muntner *et al*., 2014, Bild *et al*., 2002). It can help clinician to the estimate the CVD risk and recommendation of statins for non-diabetic patients (LDL 90-189 mg/dl) and pooled cohort risk score ≥7.5%. It is generally being observed that the patients having lower threshold of 7.5% have more towards statins therapy however some studies advocate otherwise. It has also been concluded that lower risk patient (<7.5%) have higher ASCVD risk (Vergouwe and Steyerberg, 2002, Johansen *et al*., 2014).

In this study we determine the risk in individuals and evaluate the association risk with Age, gender, SBP and TC. We concluded that the patients having strong association and high OD have more risk and need to HIS and MIS therapies. RPCE risk score should be compared with Framingham risk score for better and magnified results.

CONCLUSION

CVD risk prediction is significant to know for avoiding the silent death. Prevention is better than cure for the ones who know that they are at risk. By following AHA guidelines, heart risk can be minimized and further quality of life can be improved by use of moderate to high level statin along with life style modification. For more magnified result FRS score would be compare with RPEC for recommendation of statins.

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