



Original Research Article

Cardiovascular risk assessment in general population at primary health care centers in Saudi Arabia: Using the World Health Organization/International Society of Hypertension risk prediction charts

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Recent researches have used cardiovascular prediction risk score to estimate total cardiovascular disease (CVD) risk in the population. Most of these prediction charts are country and ethnic specific, which may not be reliable in different community. This study aimed to estimate the prevalence of CVD risk prediction among adults aged above 40 years, utilizing the World Health Organization / International Society for Hypertension (WHO/ISH) risk charts. A cross-sectional community based study was conducted between April to December 2016, in three regions of Saudi Arabia. Three primary health care centers selected randomly from each region and each center randomly selected 100 participants aged between 40-79 years from its database. The study involved medical history, physical examination and estimation of 10 years risk using WHO/ISH. The study included 809 adults above 40 years of age with female preponderance of 65.1%. The mean age for male was 58.16±10.6 and 55.52±8.78 for female with a p-value 0.001. Sixty nine percent of the participants were at low risk group while 31% were at moderate and high-risk group. Risk levels among diabetes by gender using cholesterol and non-cholesterol charts showed significance with p-value of 0.025 and 0.01 respectively. To conclude, known people based on risk prediction chart in primary health care centers is a step forward to have clear idea about magnitude of the problem. This study revealed the burden of CVD risk in the community. Measurement of total CVD risk offers a distinct advantage to monitor impact of multi-factorial interventions overtime and to assess total preventive treatment needs.

Key words: Saudi Arabia, primary health care, cardiovascular disease, Non-communicable diseases, WHO/ISH Risk Prediction Chart.

INTRODUCTION

Cardiovascular disease (CVD) is a leading cause of morbidity and mortality worldwide. It accounts for approximately one third of all deaths (WHO, 2010). Prevention of people with increased CVD risk requires to follow healthy diet, active lifestyle, or drug interventions. Cardiovascular disease constitutes one of the major causes of deaths and disabilities, globally claiming 17.3 million

lives a year. Incidence of CVD is expected to rise to 25 million by 2030, and Saudi Arabia is not an exception. Heart disease and stroke, accounts for almost half of all NCD-related deaths in low- and middle-income countries. The World Health Organization (WHO) estimated that, out of 17.3 million CVD deaths globally, heart attacks and strokes were responsible for 7.3 and 6.2 million deaths respectively

(Mendis et al., 2011). According to the INTERHEART and INTERSTROKE studies, hypertension, diabetes, dyslipidaemia, obesity, smoking, physical inactivity, poor diet, and alcohol consumption are the most common risk factors for heart attacks and strokes worldwide (O'Donnell et al., 2011; Yusuf et al., 2004).

The rapid socioeconomic growth in the Gulf countries lead to a change in lifestyle with increased consumption of unhealthy food and sedentary lifestyle, and as a consequence increased CVD and associated risk factors among Saudi population (Mabry et al., 2010).

The rate of CVD deaths in Saudi Arabia, UAE, Bahrain, and Qatar are; 42%, 38%, 32%, and 23%, respectively (WHO, 2011). The Saudi Project for Assessment of Coronary Events (SPACE) reported that ischemic heart disease was present in 32% of the study population. The study also reported that diabetes (56%) is the most common risk factor for coronary heart disease (CHD), followed by hypertension (48%), current smoking (39%), and hyperlipidemia (31%) (AlHabib et al., 2009). World Health Organization - Noncommunicable Diseases (NCD) Country Profiles reported that over 42% of all deaths are attributed to CVD in Saudi Arabia (WHO, 2014).

As most people who develop atherosclerotic cardiovascular disease have several risk factors, which interact to produce their total risk, it is recommended to assess individual's total burden of risk in clinical practice rather than on the level of a particular risk factor (Robson and Feder, 2001; Pearson et al., 2002; Jackson, 2000).

A Danish study using Framingham risk screen concluded that there was a significant over estimation of coronary risk on the population. The validity of risk scores developed for population with different incidence of the disease should preferably be tested prior to application (Thomsen et al., 2002). Moreover, study applying Framingham risk function to data from Danish and German prospective studies have demonstrated that the Framingham risk function clearly overestimates coronary heart disease risk in their populations (Hense et al., 2003). In the gulf region, a study contacted in Oman found that Framingham risk screen overestimated the number of patients eligible for primary prevention compared with the WHO/ISH risk charts (Al-Lawati et al., 2013).

Since the publication of the first risk scores from the Framingham Heart Study in 1976 (Kannel et al., 1976), many scores have been developed and are in use from other cohort studies, mainly in developed countries involving Caucasian populations (Assmann et al., 2002; Hippisley-Cox et al., 2007; Ferket et al., 2010). The scores vary widely in terms of study characteristics, predictors and CVD outcomes investigated (Jones et al., 2001). Risk scores based upon studies conducted in high-income countries may not be suitable for use in low-resource settings.

Therefore the World Health Organization and the International Society of Hypertension (WHO/ISH) developed sets of regional risk prediction charts based on fewer risk factors that can be assessed by physicians and

non-physician health workers in primary care setting for CVD prevention in each of the fourteen WHO sub-regions (WHO, 2007)

Although the CVD risk scores are designed for use by clinicians for quick and consistent estimation of total CVD risk in individuals, these can also be used to estimate and monitor population distribution of CVD risk from cross-sectional survey (Mendis et al., 2011; Ndindjock et al., 2011).

National health planners may use population distribution of total CVD risk to assess total preventive needs and associated costs as well as to monitor net effectiveness of interventions that affect multiple CVD risk factors by different magnitudes and direction (Batsis and Lopez-Jimenez, 2010).

This study aimed to estimate the prevalence of CVD risk among adults aged above 40 years, utilizing the World Health Organization / International Society for Hypertension (WHO/ISH) risk prediction charts.

METHODOLOGY

This is a descriptive cross-sectional, community-based study. It was conducted between April to December 2016, in three regions of Saudi Arabia (Western region-Jeddah; Eastern region-Alhasa and Northern region-Arar). National Ethical Review Committee Ministry of Health approved the study.

Three primary health care centers were selected randomly from each region, and; each center randomly selected 100 participants aged between 40-70 years from its database. Participants had verbal explanation of the study and verbal informed consent obtained. Individuals interviewed to elicit information on demographic and socio-economic characteristics, tobacco, dietary intake, physical activity, and history of hypercholesterolemia, diabetes and hypertension.

Participants with history of heart or kidney failure, stroke, liver diseases and pregnant women were excluded.

The study used WHO/ISH risk prediction charts which indicate 10-year risk of a fatal or nonfatal major CVD cardiovascular event (myocardial infarction or stroke). It includes age (years), sex, systolic blood pressure (mmHg), total cholesterol (mmol/l), smoking status and presence or absence of diabetes mellitus for 14 WHO epidemiological sub-regions. We used the Eastern Mediterranean B subgroup (EMR B) which are region, country and income specific (WHO, 2007)

Cholesterol and Non-cholesterol charts used for all participants to compare the finding between them.

For total CVD risk calculation, a person was categorized as smoker who are smoking currently or quitted smoking less than one year. Diabetes defined as fasting blood glucose ≥ 7.0 mmol/l, 126 mg/dl, or person on diabetic medication. Using electronic sphygmomanometer (Omron Corporation, Japan), systolic blood pressure was measured; the mean of three reading

Table 1. Baseline characteristics of the study population

Characteristic		No.	%	P value
Gender (n=809)	Male	282	34.9%	
	Female	527	65.1%	
Age (n=808)	Male (n=282)	58.16±10.6		0.001<
	Female (n=526)	55.52±8.78		
BMI (n=768)	Male (n=277)	33.45±6.9		NS
	Female (n=492)	33.68±7.9		
Systolic BP mm Hg (n=808)	Male (n=282)	134.5±16.7		NS
	Female (n=526)	132.8±18.6		
Performing Physical exercise (n=796)	Do not exercise	255	33.2%	NS
	Occasional exercise	347	43.6%	
	Regular exercise	194	24.4%	
Smoking status (n=801)	smokers	70	8.7%	0.001<
	Non-smokers	731	91.3%	

Table 2 Cardiovascular diseases Risk level by age

Risk level	Age in Categories								Total
	40-49.9 Years		50-59.9 Years		60-69.9 Years		70-79.9 Years		
	n	%	n	%	n	%	n	%	
Low Risk	186	95.3	278	91.7	83	36.7	13	15.3	560
Moderate Risk	7	3.6	21	6.9	111	49.1	54	63.5	193
High Risk	2	1.0	4	1.3	32	14.2	18	21.2	56
Total	195	100	303	100	226	100	85	100	809

was taking for the study. Total cholesterol level was taking as a mean of two non-fasting measures in the last two months.

The risk categories for 10-year total risk of a fatal or non-fatal CVD event include <10% classified as "Green", 10 - <20% "Yellow", 20 - <30% "Orange", 30 - <40% "Red" and ≥ 40% "Deep Red" (WHO, 2007).

This study grouped the five categories into three groups <10% "Low Risk", 10% - <30% "Moderate Risk" and 30% - ≥ 40% "High Risk".

Practice notes accompany WHO/ISH risk score charts for clinicians to aid interpretation and adjustment of individuals' risk factors were included in the risk score calculation (WHO, 2007; Cooney et al., 2010).

Data analysis

Statistical analysis was done using performed using SPSS (version 20) for data cleaning, management, and analyses. Categorical variables were summarized by calculating the number and percent, whereas the mean and standard deviation were calculated for continuous variables. Comparison of the two groups analyzed by using Chi-square test for categorical variables, and the student's t-test for continuous variable. A p-value ≤ 0.05 was considered to be statistically significant.

RESULTS

Demographic characteristics of the participants (809) Table 1, reveals that 34.9% was male and 65.1% female. The mean age was 58.16±10.6 and 55.52±8.78 in male and female respectively with a significance P value < 0.001. The mean BMI for male was 33.45±6.9 and 33.68±7.9 for female. Although not significant female showed higher BMI among the age group 50-70 years.

The prevalence of smoking was higher in male than female. Seventy percent (70%) were performing physical exercise at least once a week. Family history of CVDs reported in 17.5%.

Table 2 Analyzing age groups across the three CV risk level (low risk < 10% - moderate risk 10% - <30% - high-risk 30% - ≥ 40%); showed the trend of increasing moderate and high-risk group with age.

Table 3 reveals the analysis of the two WHO/ISH risk prediction charts comparing with gender. Risk level among diabetes using cholesterol and diabetes without cholesterol charts showed significance with p-value of 0.025 & 0.01 respectively, while the non-diabetic group showed no significance.

Table 4 showed risk factors in the study group which are not included in the prediction charts. Obesity and physical exercise were 69% in the low risk (< 10%). On the other hand, the hypertensive participants on treatment were

Table 3 Risk Level among Different Groups by Gender

Risk level	Chart with cholesterol measurement				Chart without cholesterol measurement			
	Risk level among diabetics		Risk level among non-diabetics		Risk level among diabetics without cholesterol measure		Risk level among non-diabetics without cholesterol measure	
	Male	Female	Male	Female	Male	Female	Male	Female
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Low Risk	79 (53)	134 (66.7)	32 (68.1)	50 (83.3)	30 (60.0)	94 (63.9)	33 (91.7)	107 (89.9)
Moderate Risk	35 (23.5)	41 (20.4)	10 (21.3)	7 (11.7)	13 (26.0)	35 (23.8)	3(8.3)	10(8.4)
High Risk	35 (23.5)	26 (12.9)	5 (10.6)	3 (5.0)	7 (14.0)	18 (12.2)	0 (0)	2 (1.7)
Total	149 (100)	201 (100)	47 (100)	60 (100)	50 (100)	147 (100)	36(100)	119(100)

Table 4 Risk factors not included in the scoring system WHO/ISH

Risk factors	Combined Risk			P value
	Low	Moderate	High	
Obesity (768)	532 (69.3%)	184 (23.9%)	52 (6.7%)	Not significant
Physical activity (796)	552 (69.3%)	189 (23.7%)	55 (6.9%)	.000
Personal history of CVD (799)	33 (4.1%)	28 (3.5%)	14 (1.7%)	Not significant
Family history of CVDs (795)	90 (11.3%)	40 (5.0%)	10 (1.3%)	Not significant
Smoking (802)	40 (5.0%)	21(2.6%)	9 (1.1%)	
Hypertensive on treatment (800)	285 (35.6%)	141 (17.6%)	55 (6.9%)	0.000

Table 5 comparison of cholesterol/non- cholesterol charts among the same individuals

Risk level	The same diabetic individuals				The same non-diabetic individuals			
	Cholesterol Measure included		Cholesterol Removed		Cholesterol Measure included		Cholesterol Removed	
	n	%	n	%	n	%	n	%
Low Risk	213	60.9	225	64.5	82	76.6	85	79.4
Moderate Risk	105	30.0	95	26.9	23	21.5	21	19.6
High Risk	32	9.1	30	8.6	2	1.9	1	0.9
Total	350	100	350	100	107	100	107	100

35.6% in low risk group.

In the current study, Table 5 reveals the comparison of the same individuals using both WHO/ISH charts with and without cholesterol. The study showed no significant change in using either charts.

DISCUSSION

In accordance with current study and previous studies clearly stated that most NCDs result in CVDs due to a combination of multiple risk factors (WHO, 2007). It documented that the eventual outcome of CVDs morbidity and mortality rarely precipitates because of a single potential risk factor, but more often because of the combined effect of several risk factors (Ferket et al., 2010).

A study in Saudi Arabia, reported that the overall prevalence of coronary artery diseases is 5.5% (Cooney et al., 2010; Al-Nozha et al., 2004). Health Information Survey conducted by the Ministry of Health, Saudi for Non-

Communicable Diseases in 2013 showed that the prevalence of CVDs was 46% (WHO, 2014).

Studies have revealed that the cardiovascular risk evaluation by general practitioners is limited and thus there is immense need to enhance their awareness of the importance of scoring the 10-year prediction (Cooney et al., 2009).

Multiple studies across the world have utilized the WHO/ISH cardiovascular risk prediction charts to estimate the risk in heterogeneous settings (Mendis et al., 2011; Kuklina, 2010; Koju et al., 2011).

In the present study, utilizing WHO/ISH risk prediction charts high-risk participants were 6.9%. Various studies have revealed a variable level of prevalence of CVD risk using the similar WHO/ISH risk prediction charts. In Asian countries: China 1.1%, Iran 1.7%, Sri Lanka 2.2%, Nepal 9.8%, and Pakistan 10.0% (Mendis et al., 2011; Koju et al., 2011). reported less than 10% in high-risk subjects. On the other hand, Malaysia reported (21.5%) (Otgontuya et al., 2013), other studies in Africa reported 5.1 % and 5%

in Seychelles and Nigeria respectively (Ndindjock et al., 2011)

Recent studies in the region used the WHO/ISH risk prediction charts in selected diabetic patient, resulted in 17,1% and 20% of patient having CVD risk of $\geq 20\%$ over 10 years in Saudi Arabia and Oman respectively (Al-Lawati et al., 2013; Mohammed et al., 2017). This study revealed 17.4% diabetic patients were having $\geq 20\%$ over 10 years.

The current study compared WHO/ISH risk prediction charts with cholesterol and non-cholesterol in all individuals of the study population. The study concluded that there was no significant change in using either chart.

These risk prediction charts has been identified as a key tool in the successful implementation of the NCD action plan (WHO, 2014). These findings point that although WHO/ISH risk charts are a handy and simple tool for CVD risk prediction, but may underestimate the CVD risk burden. The CVD risk factors relevant to our community like obesity, family history of CVDs, smoking, high salt intake, and NCD treatment status are not part of the current risk prediction chart.

The finding of the study revealed the high burden of CVD risk in the country. Risk scores, which estimate an individual's total CVD risk, can help to ensure that individuals with high total score will receive preventive and curative treatment irrespective of no high a single risk factor.

Physicians in primary health care have to change the attitude of treating single risk factor to total risk, which will save cost without sacrificing health benefits. The finding of no difference between the charts, which include or exclude cholesterol, this will help PHC physician in remote area to use the available charts depending on their facilities.

Finally, we recommend health staff to apply WHO/ISH risk prediction charts to all subjects who have NCDs to evaluate their risk factor.

To conclude, known risk prediction of people is a major step to have a clear idea about the magnitude of the problem and in return early management. The finding of the study revealed the high burden of CVD risk in the country.

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Competing interests

Authors declare that they have no competing interests.

REFERENCES

- AlHabib K, Hersi A, AlFaleh H, Kurdi M, Arafah M, Yousef M (2009). The Saudi Project for Assessment of Coronary Events (SPACE) registry: design and results of a phase I pilot study. *Can J Cardiol.*; 25(7): e255–e258.
- Al-Lawati J, Barakat M, Al-Lawati N, Al-Maskari M, Elsayed M, Mikhailidis D (2013). Cardiovascular Risk Assessment in Diabetes Mellitus: Comparison of the General Framingham Risk Profile versus the World Health Organization/ International Society of Hypertension Risk Prediction Charts in Arabs--Clinical Implications. *Angiology.* 64(5):336-42.
- Al-Nozha M, Arafah M, Al-Mazrou Y, Al-Maatouq M, Khan N, Khalil M (2004). Coronary artery disease in Saudi Arabia. *Saudi Med J.* 25(9):1165–71.
- Assmann G, Cullen P, Schulte H (2002). Simple scoring scheme for calculating the risk of acute coronary events based on the 10-year follow-up of the prospective cardiovascular Munster (PROCAM) study, *Circulation.* 105(3):310-315.
- Batsis J, Lopez-Jimenez F (2010). Cardiovascular risk assessment—from individual risk prediction to estimation of global risk and change in risk in the population. *BMC Med.* 8:29.
- Cooney MT, Dudina A, D'Agostino R, Graham IM (2010). Cardiovascular risk-estimation systems in primary prevention: Do they differ? Do they make a difference? Can we see the future? *Circulation.* (122): 300–310.
- Cooney MT, Dudina AL, Graham IM. (2009). Value and limitations of existing scores for the assessment of cardiovascular risk: A review for clinicians. *J. Am. Coll Cardiol.* (54):1209–27.
- Ferket B, Colkesen E, Visser J, Spronk S. Kraaijenhagen R, E.Steyerberg (2010) Systematic review of guidelines on cardiovascular risk assessment: which recommendations should clinicians follow for a cardiovascular health check? *Arch Intern Med.* 11;170(1):27-40.
- Hense H, Schulte H, Loewel H, Assmann G. Keil U (2003). Framingham risk function overestimates risk of coronary heart disease in men and women from Germany. Results from the MONICA Augsburg cohort and the PROCAM cohort. *Eur Heart J.* 24(10):937-45.
- Hippisley-Cox J, Coupland C, Vinogradova Y, Robson J, May M, Brindle P (2007). Derivation and validation of QRISK, a new cardiovascular disease risk score for the United Kingdom: prospective open cohort study. Cite this as: *BMJ* ;335:136
- Jackson R (2000) Guidelines on preventing cardiovascular disease in clinical practice. *BMJ*(320): 659–61.
- Jones A, Walker J, Jewkes C, Game F, Bartlett W, Marshall T (2001). Comparative accuracy of cardiovascular risk prediction methods in primary care patients. *Heart.* 85(1):37–43.
- Kannel W, McGee D, Gordon T (1976). A general

- cardiovascular risk profile: the Framingham Study. *Am. J. Cardiol.* 38(1):46–51.
- Koju R, Gurung R, Pant P, Humagain S, Yogol CM, Koju A (2011). Prediction of cardiovascular disease in suburban population of 3 municipalities in Nepal. *Nepal Heart J.* (8):3–7.
- Koju R, Gurung R, Pant P, Humagain S, Yogol CM, Koju A (2011). Prediction of cardiovascular disease in suburban population of 3 municipalities in Nepal. *Nepalese Heart Journal* (8): 3-7.
- Kuklina EV (2010). Assessing and managing risk for cardiovascular disease: A worldwide perspective. *North Am J Med Sci.* (3): 94–103.
- Mabry R, Reeves M, Eakin E, Owen N (2010). Evidence of physical activity participation among men and women in the countries of the gulf cooperation council: a review," *Obesity Reviews*, 11(6): 457–464.
- Mendis S, Lindholm H, Anderson S, Alwan A, Koju R, Onwubere B (2011). Total cardiovascular risk approach to improve efficiency of cardiovascular prevention in resource constrain settings. *J. Clin. Epidemiol.* 64(12):1451-62.
- Mendis S, Lindholm LH, Anderson SG, Alwan A, Koju R, Onwubere BJ (2011). Total cardiovascular risk approach to improve efficiency of cardiovascular prevention in resource constrain settings. *J. Clin. Epidemiol* (64): 1451-1462.
- Mendis S, Puska P, and Norrving B (2011). *Global Atlas on Cardiovascular Disease Prevention and Control*, World Health Organization.
- Mohammed M, Al-Raddadi R , Alaa M, Alhaeli M , Nourah R , Mohammed I, Alsuliman Y A (2017). Cardiovascular Disease Risk Assessment among Saudi Type 2 Diabetic Patients in Jeddah City, Saudi Arabia. *Imperial Journal of Interdisciplinary Research* 3, (11ISSN: 2454-1362, <http://www.onlinejournal.in>
- Ndindjock R, Gedeon J, Mendis S, Paccaud F, Bovet P (2011). Potential impact of single-risk-factor versus total risk management for the prevention of cardiovascular events in Seychelles. *Bull World Health Organ.* 1;89(4):286-295.
- O'Donnell M, Denis X, Liu L, Zhang H, Chin S, Rao-Melacini P (2011). Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): A case-control study. *The Lancet*; 376(9735): 112-123.
- Otgontuya D, Oum S, Buckley BS, Bonita R. (2013). Assessment of total cardiovascular risk using WHO/ISH risk prediction charts in three low and middle income countries in Asia. *BMC Public Health*; 13: 539.
- Pearson T, Blair S, Daniels S, Eckel R, Fair J, Fortmann S (2002) *AHA Guidelines for Primary Prevention of Cardiovascular Disease and Stroke: Update: Consensus Panel Guide to Comprehensive Risk Reduction for Adult Patients without Coronary or Other Atherosclerotic Vascular Diseases.* American Heart Association Science Advisory and Coordinating Committee. *Circulation.* (106):388–91.
- Robson J, Feder G (2001) Predicting and reducing cardiovascular risk. *Heart* (85): 487–488
- Thomsen T, McGee D, Davidsen M, Jorgensen T (2002). A cross-validation of risk-scores for coronary heart disease mortality based on data from the GLOstrup Population Studies and Framingham Heart study. *Int J Epidemiol.* (31):817-22
- WHO, *Global status report on non-communicable diseases* (2010). Geneva: World Health Organization. (http://www.who.int/nmh/publications/ncd_report_full_en.pdf)
- WHO, *Non-communicable Diseases Country Profiles* (2011). World Health Organization, Global report Geneva, Switzerland.
- World Health Organization – *Non-communicable Diseases (NCD) Country Profiles* (2014) (Saud Arabia), http://www.who.int/nmh/countries/sau_en.pdf
- World Health Organization –(2014a). *Noncommunicable Diseases (NCD) Country Profiles.*
- World Health Organization (WHO) (2014b). Target 8: Provide drug therapy to prevent heart diseases [internet]. Available from: <http://www.who.int/nmh/ncd-tools/target8/en/>
- World Health Organization. (2007) *WHO/ISH cardiovascular risk prediction charts.* http://www.who.int/cardiovascular_diseases/guidelines/Chart_predictions/en
- World Health Organization: *Prevention of cardiovascular disease* (2007). Guidelines for assessment and management of cardiovascular risk. Geneva: World Health Organization.
- Yusuf S, Hawken S, Ôunpuu S, Dans T, Avezum A, Lanan F (2004). Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study, *The Lancet.* 364(9438): 937–952.