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Country wide statistical assessment of smoking induced atherosclerotic and metabolic risk factors in Saudi population

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ABSTRACT

Cardiovascular diseases (CVD) are main cause of death in industrialized countries. Tobacco smoking is the most preventable CVD risk factor worldwide. The impact of smoking on atherosclerotic and metabolic risk factors for cardiovascular diseases among Saudi population was studied in country wide fashion. Sample population was representative, cross sectional national, aged 3064 years which is in accordance with the national population distribution with respect to age, gender, regional and residency, urban vs. rural, population distribution. Blood samples were drawn and assayed for glucose, total cholesterol, triglyceride, high density lipoprotein and low density lipoprotein. General biochemical markers such as alkaline phosphatase (ALP), creatinine kinase (CK), aspartate transaminase (AST), alanine transaminase (ALT) and lactate dehydrogenase (LDH) were assessed. The current study showed higher prevalence of atherosclerotic and biochemical risk factors in smokers compared to non-smokers Saudi subjects. Moreover, the LDH indicated higher probability for direct cardiovascular affection due to smoking habits in Saudi population. These elevated risk factors in Saudi population were found to correlate with the degree of smoking. In conclusion, We provided robust evidence based on country wide clinical analysis for the negative influence of smoking on CVD risk factor amongst Saudi population.

INTRODUCTION

Cardiovascular diseases (CVD) is a major death determinant among males and more prevalent in geriatric females in the industrialized countries [1]. The geographical distribution of CVD has been changed over the past 20 years with significant decrease in the industrialized countries and higher prevalence in the developing countries [2]. CVD constitutes of integrative risk factors such as, age, hypertension, obesity, hypercholesterolemia, smoking, insulin resistance and glucose intolerance [3, 4]. Several successful intervention maneuvers are currently implemented in the developed countries, downsizing these risk factors resulting in decreasing the prevalence of CVD [5, 6]. Pre-developing countries/transitional developing countries with respect to economical revolution have got significant rise in the incidence of CVD [7].

The Kingdom of Saudi Arabia (example of pre-developing Middle East country) has experienced significant economical breakthrough over the last two decades. Consequently, the Western life style in terms of nutritional habits and physical exercise has been adopted in Saudi Arabia. These life style changes in addition to the improved health services resulted in enhancing the longevity and the emergence of non communicable diseases such as, CVD. Significantly large proportion of hospital beds in the Kingdom of Saudi Arabia is reserved for CVD patients. Yet, It is considered the major leading cause of death over the past few years in the Kingdom [8].

Tobacco smoking is the most facile preventable CVD risk factor worldwide [9]. Currently smoking is positively associated with younger age, lower income, reduced educational achievement, and disadvantaged neighborhood environment [10, 11]. Smokers exhibit higher risk factor for cardiovascular, respiratory malignant disorders than nonsmokers [12-15]. Tobacco smoking is a powerful risk factor for incident CVD and stroke subsequent to disturbed lipid profile and progressive atherosclerosis [13]. Atherosclerosis is directly affected by the

lipids peroxidation within the extracellular matrix of vascular subendothelial spaces. These oxidized lipids, nonetheless LDL-cholesterols, activate inflammatory cascade that changes the mechanical characteristics of the arterial wall, and ultimately leads to thrombus formation [16]. Strong association between smoking and atherosclerosis was reported in various populations.

This study was designed as an Epidemiological National Cross-sectional to estimate the extend of association between the degree of smoking and glucose intolerance, hypercholesterolemia and other cholesterol related risk factors in Saudi population, aged 3064 years.

METHODOLOGY

Population selection and criteria

National Epidemiological in-house Survey for Chronic Metabolic Disorders, such as: hypercholesterolemia, diabetes mellitus, obesity and other cholesterol risk factors for CVD was performed within Saudi personnel in different territories of the Kingdom of Saudi Arabia. The objective of this study was to investigate the above mentioned risk factors for smoking among Saudi citizens aged 3064 years. A multistage stratified random cluster sampling technique was adopted to select the study population. The sample population assigned of the current study was distributed between the different territories according to the regional distribution of population as per the national population census, NPC[]. Initial adjustment was carried out for area type (rural vs. urban), population distribution in each territory according to the NPC. Villages and cities of each territory were listed and then after were randomized to select certain villages and cities according to the predesigned share of each territory in the national-wide sample. Similarly, districts within these villages and cities were randomly selected; every third parallel street in each of these locations was selected and then after every third house was included in the current study. All Saudi citizens between 3064 years old within these locations were asked voluntarily to roll-in the study.

Medical health care professionals (physicians) working in these territories were assigned and given orientation lectures for the purpose and their role in the current study, such as: filling participation forms, collecting demographic, social information and medical history. All participants were clinically investigated and those who were found free clinical diseases such as, diabetic, hypertension, liver or kidney disorders, CHD and major ECG abnormalities were included in the study. The primary care personnels were well-trained on the proper method of blood sampling, handling and measurement of height and weight. All measures were done at the Primary Care Clinic, usually couple of days, after the initial visit to the houses.

The response rate for house invitation was 92%, however, only 69% showed up in the PCC for weight, height and blood measurements. Random blood samples were withdrawn in an EDTA tube. Tubes were centrifuged and serum was stored frozen (-80 ºC) till completion of the target sample of 100 and 50 subjects per physician in each district in city or village, respectively. The samples were sent frozen to central laboratory, King Abdul-Aziz University, Jeddah, from all over the country. Samples were stored at −80° centigrade until assayed. Upon completion the target sample records were sent to central office for data entry.

Sample adjustment

Direct standardization method was carried out to adjustment the final samples; adjustment for age was carried out according to the normal national population age distribution of Saudis in compliance with the National Population Census. The known age distribution of the Saudi population permit direct and accurate adjustment of age related mortality and morbidity compared to the indirect distribution that involves calculation based on the world standard population distribution, particularly, in view of the high prevalent obesity and diabetes mellitus.

After complete data entry, another final adjustment was carried out for regional distribution (urban vs. rural), age and gender throughout the whole random selection. The final normalized sample for citizens within the age of 3064 years was found to be a total of 2049 subjects, 1016 female subjects and 1033 male subjects.

Methods

Serum glucose in the samples was assayed using glucose analyzer (Beckman Paragon, Fullerton, CA, USA). The method principle is based on the rate of oxygen consumption by glucose oxidase enzyme to convert glucose into gluconic acid and hydrogen peroxide. Oxygen rate of consumption was determined by oxygen-sensitive electrode. The glucose analyzer was calibrated immediately before assay using quality control samples provided by the manufacturing company. The values of control samples were within ±10% of the values quoted by the manufacturer. The results were presented by SI units (mmol/l). The inter-day and intra-day coefficient of variability (CV%) were 1.7% and 2.6%, respectively.

Serum lipid analysis

Total cholesterol and triglycerides analysis was undertaken using Cobas Mira S Clinical Analyzer (Roche Diagnostics) by Unimate 7 cholesterol and Unimate 7 Triglyceride, respectively.

The assay principle for total cholesterol was the enzymatic colorimetric method of cholesterol esterase and cholesterol oxidase. Triglycerides assay principle was also enzymatic colorimetric assay using glycerol phosphate oxidase enzyme. Magnesium sulphate (0.26 mol./l) was used as a precipitating agent for low density lipoprotein (LDL) cholesterol, and very low density lipoprotein (VLDL) to determine the high density lipoprotein (HDL) cholesterol. HDL cholesterol was determined by an enzymatic colorimetric method. LDL cholesterol was estimated by using the formula: LDL cholesterol=total cholesterol − (HDL cholesterol + 0.46 × triglyceride). The intraday and inter-day assay coefficients of variation were 2.6% and 2.2%, for total cholesterol, respectively; and 2.2% and 2.2% for triglyceride, respectively [17, 18].

Biochemical assessments

Biochemical assessments were assessed in isolated sera using specific kits purchased from Dade Behring, Marburg, Germany. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were assessed as previously described [19].

Creatinine kinase (CK), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH) were determined in sera using the manufacturer standard operating protocol of the kit.

Statistical analysis

Student t-test of significance was used to calculate the degree

Table 1. The significance level in serum glucose and lipid profile between smokers (light and heavy) and normal Saudi healthy population

	Fasting status		Non fasting status	
	Light smokers	Heavy smokers	Light smokers	Heavy smokers
Glucose	(+) 0.1452	(+) 0.0762	(+) 0.10541	(+) 0.05914
Cholesterol	(+) 0.076	(+) 0.008	(+) 0.06293	(+) 0.00208
LDL-c	(+) 0.3961	(+) 0.1284	(+) 0.01304	(+) 0.00244
HDL-c	(-) 0.0262	(-) 0.0088	(-) 0.00930	(-) 0.00626
TG	(+) 0.0252	(+) 0.0016	(+) 0.00389	(+) 0.00016

1 level of significance is calculated using student t-test and the calculated t-values are included in the table
2 the sign (+) indicate increased level and the sign (-) indicate decreased level compared to control group

Table 2. The significance level in serum biochemical markers between smokers (light and heavy) and normal Saudi healthy population.

	Fasting status		Non fasting status	
	Light smokers	Heavy smokers	Light smokers	Heavy smokers
ALP	0.2902	0.0131	0.0372	0.0207
CK	0.0350	0.0212	0.0908	0.03003
AST	0.1430	0.0258	0.1326	0.0336
ALT	0.467	0.0177	0.0188	0.0013
LDH	0.0307	0.0263	0.0326	0.0272

1 level of significance is calculated using student t-test and the calculated t-values are included in the table

of significance between each smoking group and control group. Data is expressed as the calculated t-value determined using SPSS® for windows, version 17.0.0.

RESULTS

Study demographic characteristics.

There were 1016 female subjects and 1033 male subjects with average age of 41.6±9 and 42.4±9.6 years, respectively.

Influence of smoking on body mass index (BMI), lipid parameters and serum glucose in Saudi population.

The calculated t-value was taken as parameter for probability assessment in the current study. No significant difference in mean BMI was detected between different groups, either male or female subjects. Within the same group, no significant difference of BMI between male and female subjects was observed.

There was no significant difference of means of serum total cholesterol, TG, LDL-c and HDL-c concentrations between male and female subjects for any group except females older than 45 years old. Under fasting condition, there was a progressive increase in probability of elevated serum TC and LDL-c risk with steady decline in the protective ability of serum HDL-c for all subjects with progressive smoking habit. The t-values for light smokers were lower than these of heavy smokers in all lipid

profile parameters reaching the level of universal significance ($p<0.05$) only in HDL-c and TG. In heavy smokers group, all lipid parameters except total cholesterol were significantly different from non-smoker subjects ($p<0.05$). With respect to random non-fasting blood sampling condition, the progressive significance of deteriorated lipid profile was more obvious showing lower calculated t-value compared to non-smokers. All detailed lipid profile parameters (LDL-c, HDL-c and TG) reached the universal level of significance ($p<0.05$) compared to non-smokers with random blood sampling (Table 1).

Serum glucose level, as well, showed progressive increasing trend with the degree of smoking. However, neither fasting nor random glucose level reached the level of universal significance ($p<0.05$) between any group and non-smokers (Table 1).

Influence of smoking on some important biochemical parameters in Saudi population.

In the current study, we assessed several muscle (ALP and CK), kidney (CK), liver (ALP, AST and ALT) and cardiac muscle related (LDH) biochemical markers in smoking (light and heavy) and non-smoker Saudi population. In light smokers, ALP, CK, AST and LDH showed trend of elevation indicative of kidney, liver and cardiac muscle affection. However, this change did not reach the universal level of significance ($p<0.05$). Only ALT and LDH showed significant elevation in light smokers compared to non-smokers which are indicative of mild hepatic and cardiac muscle affection, respectively. In contrast to lipid profile, fasting and non-fasting condition did not significantly impact the conclusion drawn from these parameters in Saudi population. In heavy smokers group, the probability of these target organ affection was greatly increased. Significant elevation in all biochemical parameters was detected with t-value exceeding the universal level of significance ($p<0.05$) (Table 2).

DISCUSSION

Metabolic risk factors for CVD such as: obesity, diabetes mellitus, hypercholesterolemia, cholesterol related risk factors and smoking among Saudi subjects, were the focus of this population based study.

Obesity is recognized as a key risk factor for CVD. It is widely prevalent among Saudi citizens, nonetheless, female subjects. The 90th percentile of BMI for Saudi citizens is higher than their corresponding European subjects within the same age and gender categories [20]. The obesity in Saudi Arabia is the highest around the world [21, 22]. The overweight/obesity ratio is dangerously low in the Kingdom of Saudi Arabia, when compared with developed countries. In Saudi Arabia, the overweight to obesity ratio is 35% and 7%, respectively for male citizen (ratio = 5), while for female subjects 24% and 8%, respectively (ratio = 3). This low ratio within Saudi population probably reflect the lack of understanding the importance of early intervention at the stage of overweight with proper maneuver before proceeding frank obesity state [23]. It might also reflects how obesity is perceived as well-being health state among Saudi citizens [24].

The 90th percentiles of serum total cholesterol concentration for Saudi subjects were lower across all age groups than sex and age corresponding European citizens [20]. In addition, Hypercholesterolemia for Saudi subjects was lower than hypercholesterolemia for age and sex corresponding citizens from countries, such as USA and Turkey [25, 26].

Low level of HDL (less than 0.9 mmol/l) is indicative for positive risk factors prevalence, when compared with other country such as Seychelles Island. This country shares similar prevalence of obesity and hypercholesterolemia with Saudi Arabia [27].

A large number of female subjects were found to be free of risk factors categorized between the ages of 3039 years. This ratio was found to decline in older age categories approaching the same risk status of male citizens. In the age category of 3039 years, there was large percentage of male subjects with one risk factor (most commonly smoking). On the other hand, the most common single risk factor among female subjects was obesity; which was more prevalent after age of 40 years. There was more male subjects with two risk factors between the ages of 3039 years; most commonly, smoking and obesity.

The interrelation between smoking and cardiovascular diseases and/or their biochemical markers have been reported before, however, to a lesser extent within Saudi population [9, 13, 28-30]. Herein, the assessment of early statistical evidence regarding the relation between CVD risk factors and tobacco smoking was proved in Saudi population in country wide study. Not only the smoking *per se* was studied, but also the degree of smoking was correlated to atherosclerotic risk factor in Saudi population.

CONCLUSION

We provided robust evidence based on country wide clinical analysis for the negative influence of smoking on CVD risk factor amongst Saudi population.

Conflict of interest

Authors do not have any financial conflict of interests.

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