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Risk Factors of Type 2 Diabetes and Cardiovascular Diseases among Saudi Arabian Adolescents

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Abstract: This study aimed to investigate the prevalence of risk factors for Type2 Diabetes and Cardiovascular Diseases among Saudi Arabian adolescents of Arar region. A descriptive epidemiological cross sectional study was conducted with 200 participants (aged 14-19 years) randomly selected from secondary and high schools in the northern border region, KSA. Fasting blood glucose (FBG), total cholesterol (TC) and triacylglycerols (TG) serum levels along with glycated hemoglobin (HbAlc) for early screening of risk factors for T2DM and CVDs in the school setting. FBG, HbAlc and TG mean levels were significantly higher in female subgroup when compared to those of male subgroup. Our results revealed that 68 (34%) of our participants were over weighed, 56 (28%) were class I obese, 40 (20%) were class II obese and 14 (7%) were class III obese. There was a significant positive correlation between BMI and HbAlc ($r = 0.33$, $p<0.001$). In addition, there was a borderline significance regarding correlation between abdominal obesity and blood pressure ($r = 0.2$, $p = 0.05$). Significant correlation of family history of diabetes with higher body mass index measurements and total serum cholesterol levels was observed. Advanced degree of obesity (class II and III) showed statistically significant higher levels of both blood glucose and HbAlc levels when compared to other subgroups ($p = 0.021$ and 0.29, respectively). Obesity was associated with an adverse biomarker profile for CVD and type 2 diabetes. Intense and stringent preventive measures directed towards reducing the risk factors, particularly obesity, can result in reasonable reduction of disease prevalence.

Key words: Risk factors, T2DM, CVD, Northern border region, KSA

INTRODUCTION

Obesity and related risk factors of type 2 diabetes (T2D) and cardiovascular diseases (CVDs) are of major public health concern, especially in resource-limited countries where the healthcare costs of chronic diseases are increasing (Berry *et al.*, 2006).

T2DM is the most common type of the disease, accounting for around 85-95% of all diagnosed cases of DM (Ekoe and Zimmet, 2001). The diagnosis of T2DM usually occurs after the age of 40 years, but can occur in younger adults and even children. People with T2DM can remain asymptomatic for many years and the diagnosis is often made incidentally or when complications occur (WHO, 2011). In contrast to type 1 DM, T2DM patients are not dependent on insulin therapy and are not prone to ketosis, but may require insulin for control of their hyperglycemia if this is not achieved with diet alone or with oral hypoglycemic agents (Ekoe and Zimmet, 2001).

The etiology of T2DM is complex and is known to be multifactorial. T2DM is associated with several risk factors which influence the disease occurrence, but are not necessarily be the causal factors. These risk factors can be demographic (e.g. age), genetic, or behavioral (e.g., obesity, physical inactivity, diet, smoking). Behavioral risk factors are often known as 'modifiable risk factors', as changes to these factors could change the disease occurrence in high-risk individuals (Rewers and Hamman, 1995).

Reports on lack of adequate physical activity and imbalance in dietary patterns among the Saudi population are hard to be obtained and to measured accurately. It is generally known that even in more developed countries assessment of physical activity and dietary patterns in population studies have been observed to be constraining as there are variations in the methods of measurement of these two conditions and most of such methods are of highly 'subjective' nature (National Obesity Observatory, 2013).

WHO consultation report recommended that glycated haemoglobin (HbA1c) can be used as a diagnostic marker for diabetes.43 As the average amount of plasma glucose increases, the fraction of HbA1c also increases, so that it serves as a marker for average blood glucose levels over the previous period (8-12 weeks) prior to the measurement. An HbA1c of 6.5% is recommended as the cut point for diagnosing diabetes. A value of less than 6.5% does not exclude diabetes diagnosed using glucose tests (WHO consultation report, 2011).

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Obesity is a complex multifactorial chronic disease that develops from an interaction of genotype and environment. It involves the integration of social, behavioral, cultural, physiological, metabolic and genetic factors (Al-Quaiz and Al-Joharah, 2001). Adolescents in developing countries are consuming more high-fat, energy-dense foods and engaging in decreased physical activity, which mimic the lifestyle of developed nations (Prentice, 2006).

The majority of cardiovascular disease (CVD) is caused by risk factors that can be controlled, treated or modified, such as high blood pressure, cholesterol, overweight/obesity, tobacco use, lack of physical activity and diabetes. However, there are also some major CVD risk factors that cannot be controlled. In terms of attributable deaths, the leading CVD risk factor is raised blood pressure (to which 13% of global deaths is attributed), followed by tobacco use (9%), raised blood glucose (6%), physical inactivity (6%) and overweight and obesity (5%) (Global Atlas on Cardiovascular Disease Prevention and Control, 2001). So the aim of the present study was to investigate the prevalence of risk factors for T2DM and CVDs among Saudi Arabian adolescents in Arar region. Data collected have been used in reducing the prevalence of these risk factors through encouraging and supporting healthy behaviors and early detection services.

MATERIALS AND METHODS

General data: A descriptive epidemiological cross-sectional study was conducted on 200 participants from both sexes (aged 14-19 years) randomly selected from secondary and high schools in northern borders area of KSA to assess the risk factors of T2DM and CVDs such as overweight and obesity, high levels of fasting blood glucose (FBG), glycated hemoglobin (HbAlc), total cholesterol (TC), blood pressure (BP), waist circumference (WC), waist to height ratio (WHtR), family history of overweight and poor dietary intake. This was executed by structured questionnaire asking about the socio-demographic data and the risk factors. Both normal and overweight adolescents were included in the study. Only subjects who weighed over 50 kgs and were in apparent good health had their blood drawn by venipuncture. Subjects were excluded from the study for the following reasons: individuals on medications known to alter blood pressure, glucose or lipid metabolism and if they had known eating disorders.

The overweight was defined as BMI $\geq$25 kg/m^2 and obesity was defined as BMI $\geq$30 kg/m^2. Furthermore, obese adolescents were categorized into class I (BMI; 30-34.9), class II (BMI; 35-39.9) and class III (BMI $\geq$40) (WHO, 2000). Waist to height (cm) ratio WHtR, in addition, was calculated as "the ratio of waist (cm) and height (cm)". Abdominal obesity was defined as a WhtR >cutoff of 0.5 for both 14-19-year-old boys and girls (Abolfotouh *et al*., 2011). Risk factors include: Waist circumference (cm) ($\geq$94 Male, $\geq$80 Female), Waist-to-height ratio ($\geq$0.5 both gender), Fasting blood glucose ($\geq$5.5 mmol/l), HbA1c (>6.5%), Total cholesterol (>4.5 mmol/L), Systolic BP (>140 mmHg), Diastolic BP (>90 mmHg), BMI (>25) and positive family history. We classified individuals according to the number of risk factors they have as individuals have no risk factors (0), one risk factor (1), two risk factors (2), three risk factors (3), four risk factors (4), five risk factors (5).

Blood sample collection: Blood samples were taken after a 10 h fasting by stuff nursing, used needle prick from thumb in schools and then analyzed by Reflotron plus apparatus to measure FBG, TC and TG. This *in vitro* diagnostic device works on the principle of the reflective photometry to determine blood chemistry results. This assay had been validated previously by our group as a valid screening test (Albow *et al*., 2013). The reference range of glucose (4.1-6.2 mmol/L), Cholesterol (1.3-5.2 mmol/L) and TG (0.0 -1.7 mmol/L). One ml from the sample was placed on EDTA tube for HbA_{1c} determination (COBAS, INTEGRA, Roche Diagnostics, USA. The International Diabetes Federation guidelines of <6.5% were used as the cut-off point for normal levels of HbA1c (Bennett *et al*., 2007). Local Ethics Committee approval and written consent was obtained from the patients and the controls.

Statistical analysis: Statistical analyses were performed with Texasoft WINKS 4.651 software (Texas, USA). Continuous variables were presented as a mean±standard deviation (SD) and were compared between groups using student t-test or by one way Analysis of Variance (ANOVA) followed by Newman-keuls multiple comparisons test in case of comparison between more than two groups. Frequencies of categorical variables were expressed as "percentage" and were compared by chi-square test. "Pearson correlation coefficients" (r) were used to determine the relationship of body mass index and/or abdominal obesity and other clinical and biochemical parameters. Statistical significance was considered at $p \leq 0.05$.

RESULTS

Clinical, anthropometric, distribution of risk factors and laboratory data of the study subjects: A total of 200 adolescents (128 males and 72 females) were enrolled in the study. The percentage of risk factors in the total participants were as follow: WC (22%), WHtR (51%), FBS (15%), HbA1c (4%), total cholesterol (20%), triacylglycerols (45%), SBP (49.5%), DBP (19.5%) and obesity (89%) as shown in Table 1. And according to number of these risk factors in all individuals, we classified them into 6 groups from having no risk factors up to having 5 risk factors (Table 2). The descriptive data concerning

Table 1: Distribution of variables for the studied subjects (N = 200)

Variables	N (%)	Mean (SD)
Gender		15.8±1.5
M	128 (64)	14.3±1.2
F	72 (36)	17.3±0.9
FH of diabetes; positive		
Positive	78 (39%)	
Negative	122 (61%)	
"Body mass index"; BMI (kg/m^2)		
Normal	22 (11)	
Over weight	68 (34)	
Class I	56 (28)	
Class II	40 (20)	
Class III	14 (7)	
"Waist Circumference"; WC (cm)		78.9±13.5
No risk (<94 M, <80 F)	156 (78)	74.8±10.7
Risk (≥94 M, ≥80 F)	44 (22)	93.6±12.4
"Waist/height ratio" (WhtR)		0.49±0.08
No risk (<0.5 both gender)	98 (49)	0.44±0.04
Risk (≥0.5 both gender)	102 (51)	0.56±0.06
SBP (mm Hg)		117.9±14.1
Normal	101 (50.5)	109±12.9
Prehypertensive	90 (45)	125±7.4
Hypertensive	9 (41.5)	144±4.6
DBP (mm Hg)		70.6±9.2
Normal	61 (80.5)	68.3±d7.9
Prehypertensive	39 (19.5)	80.4±7.7
Hypertensive	0 (0)	90.4±7.9
FBG		4.6±1.07
Normal (<5.5)	170 (85)	4.3±0.82
IFG (5.6-6.9)	26 (13)	5.9±0.62
Diabetes (>7.0)	4 (2)	7.88±1.3
HbA1$_C$		5.18±0.58
Normal (≤6.5)	192 (96)	5.12±0.50
Above normal (>6.5)	8 (4)	6.73±0.05
Total cholesterol		3.82±0.89
Normal <4.5	160 (80)	3.51±0.66
Borderline (4.5-5.17)	28 (14)	4.73±0.21
High (≥5.18)	12 (6)	5.80±0.37
Triacylglycerols		1.42±0.11
Normal <1.7	100 (50)	1.52±0.12
Borderline (1.8-2.2)	70 (35)	1.83±0.13
High (≥2.2)	30 (15)	2.31±0.25

FH: Family history, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, HbA1C: Glycosylated hemoglobin A, NA: Non applicable

Table 2: Relation of the number of risk factors in study subjects (N = 200)

Number of risk factors	N (%)
0	2 (2)
1	40 (20)
2	50 (25)
3	48 (24)
4	38 (19)
5	22 (11)

the total participants and the male and female subgroups are presented in Table 3. Both subgroups were age matched. It was noted that FBS, HBA1C and TG mean levels were significantly higher in female subgroup when compared to those of male subgroup. Although total cholesterol mean level was higher in female subgroup when compared to that of male subgroup (4.4±0.83 vs., 3.5±0.78, respectively), this did not reach statistical significance (Table 3).

We found that 68 of our participants were overweight (34%), 56 (28%) were class I obese, 40 (20%) were class II obese and 14 (7%) were class III obese depending on their BMI (WHO, 2000). As shown in Table 1. Distribution of obesity subclasses among male and female subgroups was statistically insignificant.

Correlation of BMI and abdominal obesity with the clinical and biochemical parameters of the study subjects: When BMI and abdominal obesity (as assessed by waist/ Ht ratio) correlated with other clinical and biochemical parameters of the total study subjects, there was a significant positive correlation between BMI and HbA1C ($r = 0.33$, $p<0.001$) as shown in Table 4. In addition, there was a borderline significance regarding correlation between abdominal obesity and blood pressure ($r = 0.2$, $p = 0.05$) as shown in Table 5.

Clinical and laboratory parameters in relation to family history of the study subjects: Table 6 showed that participants with positive family history of diabetes, tended to have higher body mass index measurements and total serum cholesterol levels compared to those of negative one (borderline statistical significance). Although, they had in addition, higher blood glucose, HBA1C and serum TG levels, these values did not reach statistical significance.

Clinical and laboratory parameters in relation to obesity subclasses in study subjects: Different laboratory and clinical parameters were analyzed among study participants with different degree of obesity as shown in Table 7. Advanced degree of obesity (class II and III) showed statistically significant higher levels of both blood glucose and HBA1C levels when compared to other subgroups ($p = 0.021$ and 0.29, respectively). Although blood pressure readings were higher in advanced obese subclass, it was not statistically significant.

DISCUSSION

Saudi Arabia, a Middle Eastern country with an estimated population of 23 million, has undergone significant economic and cultural changes over the past thirty years. Approximately 60% of the population are urbanized and have adopted lifestyle reflecting their diet and physical activity. In Saudi Arabia the prevalence of obesity among female and, to a lesser extent, male adults has reached epidemic proportions. Obesity can be regarded as a major health problem among the Saudi population (Bahathiq, 2010).

Table 3: Clinical, anthropometric and biochemical characteristics of the study subjects

Parameter	Male group (n = 128)	Female group (n = 72)	p-value
Age (years)	15.81±1.48	15.77±1.69	0.348
FH of diabetes; positive#			
"Weight" (Kg)	68.3±20.5	49.2±12.1	0.001*
"Height" (cm)	161.6±15.1	152.5±9.3	0.003*
"Body mass index"; BMI (kg/m^2)	32.0±7.2	31.8±5.6	0.1
"Waist Circumference"; WC (cm)	82.1±13.5	73.4±11.8	0.404
"Waist/height ratio" (WHtR)	0.5±0.08	0.5±0.08	0.906
SBP (mm Hg)	117.6±14.3	125.7±11.6	0.054*
DBP (mm Hg)	70.5±9.3	74.0±8.7	0.562
FBG	4.5±0.7	4.7±1.5	<0.001*
HbA1$_C$	5.1±0.64	5.4±0.42	0.009*
Total Cholesterol	3.5±0.78	4.4±0.83	0.658
Triacyglycerols	1.1±0.49	1.1±0.82	<0.001*
Normal weight	18 (14.1)	4 (5.6)	0.759$
Overweight	42 (32.8)	26 (36.1)	
Class I	36 (28.1)	20 (27.8)	
Class II	24 (18.8)	16 (22.2)	
Class III	8 (6.3)	6 (8.3)	

FH: Family history, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, HbA1C: Glycosylated hemoglobin A, values are expressed as Means±SD or as a number (percentage). All p-values are noted in the comparison of the male group with the female group; comparisons were performed by Student *t* and #Chi-square tests. $Overall p-value for distribution of obesity type (WHO classification of obesity, 2000) regards sex. *Statistically significant (≤0.05)

Table 4: Correlation between body mass index (BMI) and other study clinical and biochemical parameters

Parameters	Pearson's r =	p-value
"Waist Circumference"; WC (cm)	0.45	<0.001*
SBP (mm Hg)	0.07	0.487
DBP (mm Hg)	0.08	0.385
FBS	0.07	0.459
HbA1C	0.33	<0.001*
Total cholesterol	0.13	0.176
Triacylglycerols	0.04	0.651

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, HbA1C: Glycosylated hemoglobin A. *Statistically significant (≤0.05)

Table 5: Correlation between abdominal obesity (Waist/height ratio) and other study clinical and biochemical parameters

Parameters	Pearson's r =	p-value
SBP	0.2	0.055*
DBP	0.2	0.046*
FBS	0.07	0.629
HbA1C	0.15	0.125
Total cholesterol	0.03	0.766
Triacylglycerol	0.05	0.602

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, HbA1C: Glycosylated hemoglobin A. *Statistically significant (≤0.05)

The present study showed that FBS, HBA1$_C$ and TG mean levels were significantly higher in female subgroup when compared to those of male subgroup. It has been suggested that differential distribution of risk factors in men and women may explain such sex differences. This explanation is supported by results of several studies from developing countries. For instance, the Turkish Diabetes Epidemiology Study showed that the prevalence of diabetes was significantly higher in women (8%) compared to men (6.2%). Authors concluded that 'lack of employment outside the home' might contribute to the higher prevalence of obesity in Turkish women. According to their study, physical activity of women in Turkey is confined to house-work and they have no tradition for sporting activities due to social and cultural restrictions (Satman *et al*., 2002).

The present study showed that 22 (11%) of our participants were normal weight, 68 (34%) were overweight, 56 (28%) were class I obese, 40 (20%) were class II obese and 14 (7%) were class III obese. There was a significant positive correlation between BMI and HbA1C (r = 0.33, p<0.001). In addition, there was a borderline significance regarding correlation between abdominal obesity and blood pressure (r = 0.2, p = 0.05). Positive family history of diabetes, tended to have higher body mass index measurements and total serum cholesterol levels when compared to those of negative one. Advanced degree of obesity (class II and III) showed statistically significant higher levels of both blood glucose and HBA1C levels when compared to other subgroups (p = 0.021 and 0.29, respectively). A previous study indicated that the overall prevalence of overweight was 10.7% and 12.7% in the boys and girls and obesity was 6.0% and 6.74% in the two groups, respectively (El-Hazmi and Warsy, 2002). The prevalence of overweight was similar to a previous study (Al-Nuaim, 1997). Another multinational study conducted in Finland, New Zealand, the United Kingdom, the United States and Western Samoa showed a large increase in prevalence, whereas some other countries showed only a slight increase (Martorell *et al*., 2000).

Table 6: Family history in relation to the clinical and laboratory parameters of the study subjects

Parameters	FH (+ve) n = 78	FH (-ve) n = 122	p-value
"Weight" (Kg)	64.5±22.2	59.4±18.5	0.198
"Height" (cm)	159.6±16.1	157.5±12.4	0.073
"Body mass index"; BMI (kg/m^2)	32.3±7.8	31.7±5.9	0.05*
"Waist Circumference"; WC (cm)	80.4±13.7	78.0±13.4	0.860
"Waist/height ratio" (WHtR)	0.51±0.09	0.50±0.08	0.307
SBP (mm Hg)	116.3±15.4	119.0±13.5	0.458
DBP (mm Hg)	68.3±9.6	72.1±8.8	0.626
FBG	4.62±0.9	4.57±1.2	0.107
$HbA1_C$	5.3±0.6	5.1±0.5	0.38
Total Cholesterol	3.88±0.78	3.71±1.0	0.043*
Triacyglycerols	1.10±0.64	1.06±0.59	0.587

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, HbA1C: Glycosylated hemoglobin A. *Statistically significant ($\leq$0.05)

Table 7: Obesity subclasses in relation to different parameters among study subjects

	Normal weight 1 (n = 22)	Overweight (n = 68)	Class I obesity (n = 56)	Class II obesity (n = 40)	Class III obesity (n = 14)	p-value
FBG	4.13±0.62	4.5±1.16	4.59±0.89	5.21±1.19	4.0±0.730	0.021*
HbA1C	4.78±0.42	5.15±0.59	5.21±0.59	5.27±0.48	5.66±0.69	0.029*
Total cholesterol	3.47±0.80	3.77±0.63	3.69±1.22	4.16±0.68	4.1±1.01	0.202
Triacylglycerols	0.97±0.39	1.12±0.89	1.09±0.46	1.10±0.48	0.99±0.27	0.956
SBP (mm Hg)	117±17.2	115±17.3	120±11.7	119±12.3	119±7.4	0.870
DBP (mm Hg)	69.2±11.3	68.9±11.2	72.3±7.4	71.4±6.8	73.3±9.4	0.745

FBG: Fasting blood glucose, HbA1C: Glycosylated hemoglobin A, SBP: Systolic blood pressure, DBP: Diastolic blood pressure. *Statistically significant ($\leq$0.05)

These significant variations in the prevalence rates in the different population groups indifferent countries may be due to both environmental and genetic factors. The type of diet, extent of physical activity and climatic conditions, all play a role in influencing overweight and obesity prevalence. In most countries, lower socioeconomic groups have a significantly lower prevalence compared to the middle or high socioeconomic groups, as well as environmental and other factors seem to play a considerable influencing role. In addition, genetic contribution is considerable, since obesity is a multifactorial complex genetic disorder (El-Hazmi and Warsy, 2002). During the last three decades Saudi Arabia has seen several changing trends in the nutritional habits and activities of children and this may be the cause of significantly high prevalence of both overweight and obesity.

The high prevalence of obesity among Saudi women could be attributed to limited physical activity as a result of the wide spread use of housemaids, the limited availability of exercise facilities for girls and women in Saudi Arabia and limited awareness in the population of the health risks associated with obesity as has proven in other areas of KSA (Bahathiq, 2010).

A cross-sectional national epidemiological household survey was carried out, consisting of 4539 Saudi subjects, over the age of 15 years. The sample was adjusted for gender, age, regional and residency and urban versus rural population distribution. Height, weight, calculation of body mass index (BMI) and random blood samples for total cholesterol measurements were determined for each subject. It was found that the mean total cholesterol for all females was significantly higher than for males (4.24 vs., 4 mmol/l) (Al-Nuaim, 1997).

CVD is responsible for over 17.3 million annual deaths; amounting to 30% of global death and is the leading cause of morbidity and mortality from non-communicable diseases worldwide. CVD-related mortality can be reduced by minimizing known risk factors. These include smoking, dyslipidemia, hypertension, diabetes mellitus, excess body weight, psycho social factors, high dietary fat intake, regular alcohol consumption and lack of physical activity (Lionel, 2007). Many of the important risk factors for cardiovascular disease are preventable through the reduction of behavioral risk factors and other specific measures focused mainly on identifying and treating individuals with increased CVD risk to prevent heart attacks and stroke (Al-Alwan *et al*., 2013).

The Kingdom of Saudi Arabia has experienced a major epidemiologic and nutritional transition in the last three decades. This is marked by economic growth, standard of living and life-style transformation, including a more sedentary lifestyle and access to higher energy-dense diet intake and increased urbanization. This transition has led to the emergence of the epidemic of non-communicable diseases and large increases in morbidity and mortality attributable to CVD. Several local studies have shown increased prevalence of diabetes mellitus (DM), smoking, obesity and hypercholesterolemia (Al-Alwan *et al*., 2013). In general, prevalence of low HDL-cholesterol and high level triglyceride is most common CVD risk factor in the Kingdom. Extremely high rates of approximately 90% have been reported both among adults and children (Al-Daghri, 2010).

Health-damaging effects of obesity have been found for mortality, cardiovascular disease, type-2 diabetes and associated risk factors such as blood pressure and lipids (Whitlock *et al*., 2009). The risk of death from ischaemic heart disease was stronger in men whose body mass index (BMI) was $\geq$27 kg/m^2 (Power *et al*., 2014).

Conclusion: Obesity was associated with an adverse biomarker profile for CVD and type 2 diabetes. Intense and aggressive preventive measures directed to reduce the levels of risk factors, particularly obesity, can result in reasonable reduction of the disease prevalence and therefore should be an urgent action. Programs to routinely screen these risk factors and improve the lifestyle of Saudi population should be implemented. High intake of fruits and vegetables in that study was associated with Significant reduction in CVD risk.

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