

A Gender-Based Approach to Cardiovascular Disease Risk Factors among Adults with Diabetes Mellitus

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Abstract:

Despite the fact that women face the lower risk of cardiovascular morbidity and mortality than men before menopause, they have the same or higher risk if they develop diabetes.

To compare the sex differences in cardiovascular disease (CVD) risk factors among adult diabetic and non diabetic patients

Case control study. The specialized center for Endocrinology and Diabetes (SCED) and outpatient Medical-Clinic at Al-Kindy Teaching Hospital, for the period from January to December-2008. 314 diabetic patients (152 males & 162 females) and 136 of non diabetic patients (72 males & 64 female) as control group. All the selected participants were adults (18 – 35) years old.

All participants were assessed for CVD risk factors, including family history, smoking status, physical activity, Body mass index, central obesity, hypertension, hypercholesteremia, hyperlipidemia and uncontrolled hyperglycemia. The gender difference between men and women, in both diabetic and non diabetic patient, had been studied.

Sex difference in CVD risk factors (hypertension, hypercholesteremia, hyperlipidemia, smoking and leisure physical activity) had been found to be statistically significant among non diabetic subjects. This significant difference was diminished in diabetic patients for all the risk factors but not for smoking habits and leisure physical activity habits.

The burden of conventional CVD risk factors in the presence of diabetes was greater in women than in men at baseline. Prospectively, hypertension, hypercholesteremia, hyperlipidemia, contributed to diabetes-related CVD risk more in women than in men.

Key words: DM, Gender, CVD

Introduction:

Cardiovascular disease (CVD) are equally important in men and women [1], yet the incidence and progression rate of cardiovascular diseases is markedly higher in men than in age matched premenopausal women [2]. In middle aged general population men have two to five times higher risk for CVD than

women [3]. The relative protection from CVD among premenopausal women is assumed to hormones [4]. The role of sex hormones in modulating the activity of several regulatory systems including the rennin – angiotensin system has been suggested [5]. Diabetes mellitus (DM) confers a markedly increased risk of CVD events in both women and men and eliminates the protective effect of female sex on the risk of

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CVD [6]. Besides, DM enhances the effect of the major CVD risk factors; smoking, hypertension, and dyslipidemia. Hyperinsulinemia to promote the atherogenic changes in blood lipids and blood coagulability and raise arterial blood pressure [4]. The pathological changes associated with atherosclerosis in diabetic patients are similar to those in the non diabetic population but occur earlier in life and are more extensive and severe [1].

Among individuals with diabetes, CVD is the leading cause of morbidity and mortality. Adults with diabetes have two to four folds higher risk of CVD compared with those without diabetes and accounted for up to two thirds of all deaths in the diabetic population [6]. According to Barrett-Connor et. al, [7] pre-menopausal women who have diabetes are at a higher risk for CVD than diabetic men.

Framingham was the first to underline that women with diabetes seem to lose their relative protection against CVD compared with men [8], and as reported by Framingham cohort study, the risk of CVD in a diabetic woman is increased by 5.4-folds, in comparison to 2.4 fold increase in a diabetic man with a trends demonstrate a modest decline in heart disease mortality in men with diabetes and an increase in heart disease mortality in women with diabetes [8].

Risk assessment is an approach to predict and estimate the risk of CVD or the effect of treatment after developing diabetes / CVD. A number of CVD risk factors have been shown to be closely related to diabetes and CVD; hyperglycemia, overweight/obesity, elevated systolic and diastolic blood pressure and dyslipidemia [6]. This assessment and identification in gender difference approach has made

it possible to develop more effective health promotion and prevention strategies that have improved women's health in many countries [10].

In light of these recommendations and the possibility of sex disparities in CVD risk factors, This study aimed to determine whether there were differences in the distribution of CVD risk factors in adult women compared with adult men with DM and matched the results with corresponding nondiabetic adult males and females.

Patients and Methods

A case – control study was conducted at The Specialized Center for Endocrinology and Diabetes (SCED) and at the outpatient clinic of medicine of Al Kindy Teaching Hospital both of them at Al Russafa directorate in Baghdad, from January to December 2008. A convenience sample of 314 adult (age from 18-35 years) diabetic (type 1 & 2) patients who were registered at the SCED center and 136 of non diabetic patients attending the outpatient clinic of Al-Kindy Teaching Hospital, were included in this study. Both groups were matched regarding their socio demographic characteristic (age, sex, residence, level of education) in order to validate the comparison process between diabetic (cases) group and non diabetic (control) group as shown in table 1.

A structured questionnaire including demographic information family history, personal history, medical history and risk factors was completed for each subject in the study group and control group. Demographic data collected include sex, age, residence (rural, urban), level of education (primary, secondary, college, higher education). Family history of hypertension and diabetes in first-degree relatives (yes, no).

Personal history ; leisure physical activity (classified as active, moderately active, and inactive based on the reported average leisure physical activity per week), and smoking habit (classified as never smoke, ex smoker, and current smoker) [11]. Medical history of diabetes mellitus and hypertension

Anthropometric measurements were calculated for all participants. Height was calculated using standing height measurement (CMS weighing equipment LTD, England). The patient stood shoeless with the heels and back in contact with the vertical column of the scale. Weight measurement with indoor clothes was done using a digital weight scale, (Seca, Australia). Before each measurement the digital scale was adjusted to zero, , and the weight was taken to the nearest fraction of Kg (to the closest 0.1 Kg) .

Body mass index (BMI) then calculated as weight (kg) divided by height squared (meter²) and was used as the criteria for diagnosis of overweight and obesity. Participants were divided into 3 groups: normal weight ($BMI < 25 \text{ kg/m}^2$), overweight ($25 \text{ kg/m}^2 \leq BMI < 30 \text{ kg/m}^2$) and obese ($BMI \geq 30 \text{ kg/m}^2$) [12].

The circumferences of waist and hip were measured and used for calculation of the waist to hip ratio (WHR). Central obesity was defined as a $WHR \geq 0.85$ for women and ≥ 0.95 for men [13].

Assessment of controlled Hyperglycemia HG by testing HbA_{1c}% level for diabetic patients. The patient whose HbA_{1c} % level 6.5% or below considered to be with controlled HG [14].

Blood pressure was measured for all participants and evaluated using a

mercury sphygmomanometer and a standard clinical protocol according to the Joint National Committee (JNC-VII) report. After 10 minutes of resting, two readings of the systolic and diastolic BP separated by 5 minutes were averaged to the nearest 2 mmHg from the top of the mercury meniscus. Systolic BP was recorded at the first appearance of sounds, and diastolic BP at phase V at the disappearance of sounds. Hypertension was defined as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg. The validity of the weight scales and sphygmomanometers was ensured by calibration prior to their use [15].

Criteria for dyslipidaemia were according to National Cholesterol Education Program adult treatment panel guidelines, and total cholesterol ≥ 200 mg/dL was considered as hypercholesterolaemia. Patients with triglycerides > 150 mg/dL, low-density lipoprotein cholesterol (LDL-C) ≥ 160 mg/dL and high-density lipoprotein cholesterol (HDL-C) ≤ 40 mg/dL were defined as having dyslipidaemia [16].

Data were collected in a personal computer and statistical analysis was conducted using Minitab statistical software package. Chi-square test was used to find the significance of variables" association in DM and non DM groups. the test with p value $0f \leq 0.05$ considered significant. While odds ratio (OR) with its 95% confidence interval (CI) was used to find the association between DM and non DM groups with the risk factors in both gender. The CI which did not contain one considered significant [17].

Table 1: The distribution of the studied sample regarding occurrence of DM and some sociodemographic criteria(age, sex, residence and education)

variable	DM (n=314) No (%)	N0 DM (n=136) No (%)	Total (N=450) No (%)	P value
Age				
18-26	148 (47.13)	76 (55.88)	224 (49.78)	0.088
27-35	166 (52.87)	60 (44.12)	226 (50.22)	
Sex				
Male	152 (48.41)	72 (52.94)	224 (49.78)	0.377
Female	162 (51.59)	64 (47.06)	226 (50.22)	
Residence				
Urban	259 (82.48)	108 (79.41)	367 (81.56)	0.44
Rural	55 (17.52)	28 (20.59)	83 (18.44)	
Educational level				
Primary	111 (35.35)	46 (33.82)	157 (34.89)	0.796
Secondary	168 (53.50)	77 (56.62)	245 (54.44)	
Higher education	35 (11.15)	13 (9.56)	48 (10.67)	

Results:

There were 152 diabetic and 72 nondiabetic men and 162 diabetic and 64 nondiabetic women in this study. The only significant sex differences among diabetic patients regarding their CVD risk factors aggregation were in their leisure physical activity ($p = 0.01$) and smoking habits ($p = 0.00$), (table 2). Among the non diabetic patients, representing the control group , a significant sex differences had been found not only in the leisure physical activity ($p = 0.03$) and smoking habit ($p = 0.00$) but also it include other CVD risk factors ; hypertension ($p = 0.027$), hypercholesterolemia ($p = 0.05$) and

hyperlipidemia ($p = 0.042$), (table 3). Family history (for DM and HT), obesity and central obesity seem to be a unique risk factors for developing CVD among both sexes in diabetic and non diabetic patients, (table 2&3)

In DM versus non DM comparison (table 4), and in male gender, the only significant odds ratio (OR) was found in family history and smoking variables, while it was not significant in all others. In female gender, the OR was significant in family history, besides, hypertension, hypercholesterolemia, and hyperlipidemia variables.

Table 2: The distribution of the DM patients regarding sex and CVD risk factors

Risk factors	Male (n=152) No (%)	Female (n=162) No (%)	P value
Family history of DM			
Yes	54 (35.53)	59 (36.42)	0.869
No	98 (64.47)	103 (63.58)	
Leisure physical activity			
Active	51 (33.55)	34 (20.99)	0.010
Moderately active	68 (44.74)	72 (44.44)	
Inactive	33 (21.71)	56 (34.57)	
Smoking status			
Never smoke	54 (35.53)	103 (63.58)	0.000
Current smoker	85 (55.92)	21 (12.96)	
Ex smoker	13 (8.55)	38 (23.46)	
Obesity			
Normal weight	61 (40.13)	47 (29.01)	0.116
Over weight	59 (38.82)	74 (45.68)	
Obese	32 (21.05)	41 (25.31)	
Central obesity			
Yes	35 (23.03)	43 (26.54)	0.471
No	117 (76.97)	119 (73.46)	
Uncontrolled hyperglycemia			
Yes	53 (34.87)	69 (42.59)	0.161
No	99 (65.13)	93 (57.41)	
Hypertension			
Yes	46 (30.26)	37 (22.84)	0.136
No	106 (69.74)	125 (77.16)	
Hypercholesteremia			
Yes	35 (23.03)	26 (16.05)	0.118
No	117 (76.97)	136 (83.95)	
Hyperlipidemia			
Yes	42 (27.63)	38 (23.46)	0.396
No	110 (72.37)	124 (76.54)	

Table 3: The distribution of the Non-DM individuals regarding sex and risk factors

Risk factors	Male (n=72) No (%)	Female (n=64) No (%)	P value
Family history			
Yes	12 (16.67)	8 (12.50)	0.493
No	60 (83.33)	56 (87.50)	
Leisure physical activity			
Active	21 (29.17)	16 (25.00)	0.038
Moderately active	36 (50.00)	22 (34.38)	
Inactive	15 (20.83)	26 (40.62)	
Smoking status			
Never smoke	14 (19.44)	39 (60.94)	0.000
Current smoker	41 (56.94)	17 (26.56)	
Ex smoker	17 (23.62)	8 (12.50)	
Obesity			
Normal weight	42 (58.33)	29 (45.31)	0.284
Over weight	18 (25.00)	19 (29.69)	
Obese	12 (16.67)	16 (25.00)	
Central obesity			
Yes	13 (18.06)	18 (28.13)	0.162
No	59 (81.94)	46 (71.87)	
Hypertension			
Yes	17 (23.61)	6 (9.38)	0.027
No	55 (76.39)	58 (90.62)	
Hypercholesteremia			
Yes	14 (19.44)	5 (7.81)	0.05
No	58 (80.56)	59 (92.19)	
Hyperlipidemia			
Yes	16 (22.22)	6 (9.38)	0.042
No	56 (77.78)	58 (90.62)	

Table 4: The distribution of risk factors in both genders regarding the presence or absence of DM.

Risk factors	Male			Female			OR ¹ \ OR ²
	DM	No DM	OR ¹ (CI)	DM	No DM	OR ² (CI)	
Family history							
Yes	54	12	2.76	59	8	4.50	0.61
No	98	60	(1.36-5.57)	103	56	(1.92-10.52)	
Leisure physical activity							
Active	51	21	1.23	34	16	0.79	1.56
Moderately active	68	36	(0.66-2.26)	72	22	(0.40-1.57)	
Inactive	33	15		56	26		
Smoking status							
Never smoke	54	14	2.23	103	39	1.12	1.99
Current smoker	85	41	(1.17-4.47)	21	17	(0.62-2.03)	
Ex smoker	13	17		38	8		
Obesity							
Normal weight	61	42	0.32	47	29	0.49	0.65
Over weight	59	18	(0.17-0.59)	74	19	(0.27-0.89)	
Obese	32	12		41	16		
Central obesity							
Yes	35	13	1.36	43	18	0.92	1.48
No	117	59	(0.67-2.76)	119	46	(0.48-1.76)	
Hypertension							
Yes	53	17	1.14	69	6	7.17	0.16
No	99	55	(0.59-2.23)	93	58	(2.93-17.58)	
Hypercholesteremia							
Yes	46	14	1.78	37	5	3.49	0.51
No	106	58	(0.91-3.54)	125	59	(1.31-9.34)	
Hyperlipidemia							
Yes	35	16	1.05	26	6	1.85	0.57
No	117	56	(0.54-2.05)	136	58	(1.22-4.73)	

Discussion:

Although CVDs are equally important in men and women, gender differences in the aggregation and progression of risk factors of the disease have been demonstrated [18]. The understanding of these differences is of crucial importance for the prediction of the cardiovascular diseases and for the development of possible new gender-specific preventive options. This approach is also of especial importance in adults diabetic patients as DM is an important known risk factor for CVD which might help to identify the similarity in potential risk among men and women.

As expected, the results of this study showed significant differences in the main CVD risk factors (hypertension, Hypercholesteremia and Hyperlipidemia) among men and women persons without DM, and because of the tradition and norms of Iraqi population, sex differences were

also found in other two of these risk factors. Firstly smoking, as our community viewed smoking as an unusual habit among women, and secondly leisure physical activity. The reason for the second exception might be explained to the restricted number of clubs and facilities where physical activity could be practiced for women and the limited activity of most women which is restricted to indoor activity only. Although a similarity in anthropometric measurements of the studied participants (men and women) manifested by obesity and central obesity could be explained by the worldwide epidemic of obesity (fostered by the modern lifestyle characterized by the lack of physical activity and an energy-dense diet) [17]. In Iraq a survey on Non Communicable Diseases (NCDS) risk factors conducted at 2006 revealed 66.9% of Iraqi population were overweight while obesity was prevalent in one third of the

population being higher among female (38.2%) as compared to male (26.2%) [19].

Among diabetic subjects, the significant sex differences for hypertension, hypercholesterolemia and hyperlipidemia were lowered down and turned into not significant. This might explain why diabetic women have the same or higher risk for CVD if they develop diabetes. According to prospective study carried in Finland they found that elevated blood pressure and atherogenic dyslipidemia contributed more strongly to diabetes related CHD risk in women than in men, beside they concluded that diabetes almost completely abolished the female protection from CHD [20].

Although the significant gender association for smoking and leisure physical activity factors were also present in diabetic patients, this might be explained as same as in those who are non diabetics. But this assessment for CVD risk factors among diabetic and non diabetic adult patients reflects the similarity in having most of these risk factors among both men and women of diabetic patients as compared with non diabetic patients which might explain why women having the same or higher risk for CVD if they develop diabetes. The two prospective population-based studies in the United States, Framingham and Evans County, that address diabetes as an independent risk factor in men and in women both suggest that diabetes predicts heart disease only in women after adjustment for covariates [21] .

The results of this study concluded that major risk factors for CVD (hypertension, hypercholesterolemia and hyperlipidemia) are aggregated in women with DM, which is also an important risk factor for CVD, as compared with non diabetic women

and appeared to have the same risk factors in CVD as adult diabetic men. This sex differences had been found among non diabetic adult patients which provide a tool for prediction of developing CVD among diabetic patients versus non diabetic. Thus more action needed to be applied and to enhance the health promotion and health protection of women among the general strategy of women health care , and the need for lifestyle modification in both male and female diabetic adult patients as primary and secondary prevention measures to prevent cardiovascular disease which is the leading cause of morbidity and mortality among diabetic .

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اعتماد الفروقات مابين الجنسين طريقة منهجية في دراسة عوامل الخطورة للإصابة بأمراض القلب والأوعية الدموية لدى المرضى المصابين بداء السكري

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الخلاصة

بالرغم من الحقيقة التي تقضي إن المرأة تواجه خطراً أقل من الرجل فيما يخص إصابتها بأمراض القلب والأوعية الدموية والوفيات الناجمة عنها قبل سن اليأس , فإنها تواجه نفس الخطورة أو أعلى في حالة إصابتها بداء السكري

لمقارنة الفروقات مابين الجنسين فيما يخص عوامل الخطورة لأمراض القلب والأوعية الدموية لدى البالغين المصابين بمرض السكري والمرضى الغير مصابين به دراسة حالة مع مجموعة ضابطة. أجريت الدراسة في المركز التخصصي لأمراض الغدد الصم والسكري وفي عيادة الباطنية / العيادة الخارجية لمستشفى الكندي التعليمي للفترة من كانون الثاني ولغاية كانون الأول 2008.

اختيرت عينة من 314 (152 ذكور و 136 إناث) من المرضى المصابين بداء السكري و 136 (72 ذكور و 64 إناث) من المرضى الغير مصابين بداء السكري كمجموعة ضابطة . مجموعتي الدراسة تم اختيارهم من اللذين تتراوح أعمارهم مابين 18 – 35 سنة تم التقصي عن عوامل الخطورة لأمراض القلب والأوعية الدموية لدى جميع المشمولين بالدراسة والتي تضمنت , تاريخ العائلة , التدخين , النشاط البدني , مؤشر كتلة الجسم , البدانة المركزية , ارتفاع ضغط الدم , ارتفاع نسبة الكوليسترول في الدم , ارتفاع نسبة الدهون في الدم , انعدام ضبط نسبة السكر في الدم . بعدها تمت دراسة الفروقات مابين الجنسين فيم يخص عوامل الخطورة لدى المصابين بداء السكري وغير المصابين.

أظهرت الدراسة وجود فروقات إحصائية معنوية مابين الجنسين فيما يتعلق بعوامل الخطورة للإصابة بأمراض القلب والأوعية الدموية (ارتفاع ضغط الدم , ارتفاع نسبة الكوليسترول في الدم , ارتفاع نسبة الدهون في الدم , التدخين , النشاط البدني) للمرضى الغير مصابين بداء السكري في حين تضاءلت هذه الفروقات لدى المرضى الغير مصابين بداء السكري لجميع عوامل الخطورة فيما عدا عملي التدخين والنشاط البدني .

تزداد عواقب عوامل الخطورة لأمراض القلب والأوعية الدموية عند الإصابة بداء السكري لدى الإناث مما هي عليه لدى الذكور وما قد ينجم عنها من مخاطر الإصابة بأمراض القلب ذات العلاقة بمرض السكري.