BENHA MEDICAL JOURNAL bmj

Print ISSN 1110-208X.

Online ISSN 2357-0016

Original article

Impact of Sex and Gender Differences on Cardiovascular Risk Factors and Cardiovascular Complications in Diabetic Patients in Benha City, Egypt: A Hospital-Based Cross-Sectional Study

Amira M. El Sayed, Walaa M. Ibrahim, Ayman M. Elbadawy, Sally H. Mohammed, Rasha O. Abd ElMoneim

Department of internal medicine, Faculty of Medicine Benha University, Egypt.

Corresponding to: Sally H. Mohammed, Department of internal medicine, Faculty of Medicine Benha University, Egypt.

Email:

s43108524@gmail.com

Received: 7 December 2023

Accepted: 5 March 2023

Abstract

Background: There is growing evidence that gender and sex differences matter when it comes to many diseases' epidemiology, etiology, treatment, and results; however, non-communicable diseases seem to be more affected by these differences. **Aims**: to investigate the effects of gender and sex variations on cardiovascular disease (CVD) risk factors and various diabetes CVD sequelae. **Methods:** A total of 1000 type 2 diabetic patients (T2DM), ages 35 to 75, were included in this cross-sectional study: 500 males and 500 females. **Results:** Diabetes duration (13.34 ± 4.64 vs. 11.99 ± 5.04 ys), HbA 1C (7.5 ± 0.55 vs. 7.28 ± 0.48 %) were considerably higher in females than males ($p < 0.001$). Waist circumference, smoking, and uric acid were significantly lower in females. BMI, total cholesterol (TC), low-density lipoprotein (LDL-C), high-density lipoprotein (HDL-C), triglycerides (TG), and family history of premature CVD were significantly higher in females. Heart failure, stroke, retinopathy, ischemic heart disease, and peripheral arterial disease were insignificantly different between both groups. While dysrhythmia, chronic kidney disease (CKD), and peripheral neuropathy (PN) were significantly lower in females than males.

Conclusions: Among Egyptian diabetic patients, Diabetes duration, family history of premature CVD, BMI, HbA 1C, TC, LDL-C, HDL-C, and TG were considerably higher in females than males. However, Waist circumference, smoking, and uric acid were significantly lower in females. Males with T2DM may be more susceptible to PN and nephropathy, whereas females with the same disease may have a lower risk of arrhythmias than men with the same disease.

Keywords: Sex, Gender, Cardiovascular, Risk Factors, Complications, Stress ECG.

Introduction:

There is growing evidence that gender and sex differences matter when it comes to many diseases' epidemiology, etiology, treatment, and results; however, non-communicable diseases seem to be more affected by these differences. Nowadays, a lot of organizations demand that the sex and gender dimensions be taken into account when conducting biomedical research in order to enhance the innovation, technology, and/or knowledge created in terms of both societal relevance and scientific quality [1].

In the areas of endocrinology and metabolism, the most considerable body of information about the therapeutic effects of sexual dimorphisms is derived from research on type 2 diabetes mellitus (T2DM). Genetic predisposition, environmental circumstances, and lifestyle decisions all contribute to the pandemic increase in T2DM and its consequences [2].

The biological differences between women and men that result from differences in sex chromosomes, sex hormones, sex-specific gene expression of autosomes, and their effects on organ systems are referred to as "sex differences." Women's bodies and hormones fluctuate more profoundly over the course of a lifetime due to reproductive circumstances [3].

Gender inequality is primarily caused by sociocultural processes, which include differences in men's and women's behavior, exposure to specific environmental factors, food habits, stress levels, lifestyles, and attitudes toward treatment and prevention [4].

Additionally, a complicated interaction between genetic, endocrine, and social variables influences gender roles and gender identity [5].

Compared with non-diabetic individuals, by 20 to 30 years old, women with T2DM had an early risk of major cardiovascular disease (CVD), and by 15 to 20 years old, for men. People with T2DM have a roughly two-fold higher stroke, myocardial infarction, and heart failure risk than people without the disease.

Women are significantly more likely than males to get a myocardial infarction due to diabetes-related extra risk, whereas both sexes with type 2 diabetes have equal excess risks for other CVDs [6].

Our study intends to evaluate gender and sex differences impact on CVD risk factors. It will also evaluate the many diabetic CVD consequences and explore potential causes and explanatory factors that may account for these variations.

Subjects and Methods:

This cross-sectional study included 1000 type 2 diabetes patients; 500 of them were male, and the remainder were female, with ages ranging from 35 to 75 years old. The study was conducted after receiving approval from the Benha University Hospitals Ethical Committee, code (MD;12-12-2020).

The study was carried out in Benha University Hospitals from March, 2021, to March, 2022.

The participants gave their informed, written consent. Patients with concomitant cardiac disorders, such as congenital heart disease, rheumatic heart disease, corpulmonale, restrictive cardiomyopathy, and hypertrophic obstructive cardiomyopathy (HOCM), were excluded, as well as those who were < 35 years of age.

Data collection:

Demographic data, a patient's history of T2DM, including duration, family history of diabetes and premature CVD, and history of diabetic complications such as microvascular (neuropathy, retinopathy, or nephropathy) or macrovascular complications (peripheral vascular disease, ischemic heart disease, or cerebrovascular diseases) were registered. Full clinical examination was performed to identify diabetic patients with CVD.

Investigations:

Fasting plasma glucose (FPG), LDL-C, TC, HDL-C, TG, serum uric acid, and kidney function tests were measured according to the laboratory's standard procedures. Whenever needed, echocardiography, resting or stress ECG, and fundus examination were performed.

Stress ECG:

The identification of coronary ischemia through an exercise stress test involves several clinical indicators. Inability to sustain six minutes of standard exercise, a failure to raise systolic blood pressure above 130mmHg, or a decrease of more than 10 mm Hg post-activity are significant. Additionally, the inability to achieve a heart rate of 85 percent of age-predicted maximum values is indicative. Electrocardiogram (ECG) signs of ischemia involve ST-segment changes—depression or elevation lasting at least 0.06 to 0.08 seconds, measuring equal to or exceeding 1 mm, and appearing horizontally or downwardly sloping. In specific cases where ST depression ascends and surpasses 1.5mm at 0.08 seconds, it signals ischemia. During stress testing, ST-segment depression commonly indicates an ischemic response, while elevation is often associated with prior myocardial infarctions and irregular left ventricle wall motion.

Occurrence of these changes within 5 minutes of exercise, the persistence of changes for more than 6 minutes into recovery, and depression in five or more leads are other markers of higher probability for coronary artery disease [7].

Sample Size Calculation:

Using the Cochran equation to obtain a 95 % confidence interval of ± 5 % around a prevalence estimate for heart failure.

Statistical analysis

Statistical analysis utilizing SPSS version 26 from IBM Inc. in Chicago, IL, USA was conducted. The unpaired Student's t-test facilitated the comparison of quantitative variables between the two groups, presenting results in mean and standard deviation (SD). For qualitative variables, frequency and percentage (%) were examined using either Fisher's exact test or the Chi-square test. A significant statistical outcome was determined by a two-tailed P value below 0.05.

Results:

Table (1) demonstrated that females had significantly greater age, diabetes duration, and HbA1c than males. The two groups' occupations, marital status, place of residence, and family history of DM did not differ significantly. Females had considerably lower fasting plasma glucose than males (P value <0.001).

Comparing both sexes (Table 2), there were insignificant differences in the systolic and diastolic blood pressure. In contrast, females had significantly lower waist circumference, smoking, and uric acid levels (P value <0.05) and significantly higher TC, HDL-C, LDL-C, TG, and family history of premature CVD than males.

Table (3) revealed that females experienced much less dysrhythmia than males did (P-value = 0.008). There was an insignificant difference in heart failure, IHD, stroke, transient ischemic attack, retinopathy, and asymptomatic peripheral arterial disease (PAD) between the two groups. Peripheral neuropathy and CKD were substantially more common in men than women (P value <0.001).

Compliance with medications was evaluated in Table 4, revealing the nonsignificant difference between both sexes in terms of anti-diabetic, anti-ischemic, anti-failure, and hypolipidemic drugs were insignificantly different.

Lifestyle features were assessed in Table 5. Compliance with a healthy diet was significantly better in males compared to females (P value=0.035). Physical activity and quality of life showed insignificant variance between both sexes.

Table (1): Demographic data and diabetes parameters in the study population:

			Males (n=500)	Females (n=500)	P value
Non-modified risk factors	**Age (years)**		56.69 ± 9.76	58.44 ± 9.85	0.005*
Modified risk factor	**Occupation**	**Worker**	310 (62%)	280 (56%)	0.054
		Not worker	190 (38%)	220 (44%)	
	Marital status	**Married**	311 (62.2%)	294 (58.8%)	0.289
		Single	189 (37.8%)	205 (41%)	
	Residence	**Urban**	325 (65%)	318 (63.6%)	0.675
		Rural	175 (35%)	181 (36.2%)	
Other parameters of diabetes					
Diabetes duration (Years)			11.99 ± 5.04	13.34 ± 4.64	<0.001*
Family history of T2DM			281 (56.2%)	307 (61.4%)	0.095
HbA1c (%)			7.28 ± 0.48	7.5 ± 0.55	<0.001*
FPG (mg/dl)			145.15 ± 11.17	137.58 ± 8.39	<0.001*

Data are presented as Mean ± SD or frequency

Table (2): Impact of sex difference on CVD risk factors:

	Males (n=500)	Females (n=500)	P value
Systolic blood pressure (mmHg)	**137.58 ± 20.45**	**136.38 ± 20.49**	**0.355**
Diastolic blood pressure (mmHg)	**79.24 ± 11.49**	**78.47 ± 11.48**	**0.292**
BMI (kg/m^2)	**29.16 ± 3.77**	**30.15 ± 3.64**	**<0.001***
Waist circumference (cm)	**101.46 ± 3.83**	**100.92 ± 4.42**	**0.038***
Smoking	**347 (69.4%)**	**190 (38%)**	**<0.001***
TC (mg/dl)	**234.87 ± 17.11**	**254.63 ± 19.5**	**<0.001***
HDL-C (mg/dl)	**28.74 ± 6.71**	**33.36 ± 7.53**	**<0.001***
LDL-C (mg/dl)	**150.63 ± 9.84**	**159.24 ± 11.7**	**<0.001***
TG (mg/dl)	**186.37 ± 11.97**	**192.26 ± 11.48**	**<0.001***
Family history of premature CVD	**<55y**	**<65y**	
	85 (17%)	**140 (28%)**	**<0.001***
Uric acid (mg/dl)	**6.43 ± 1.29**	**5.04 ± 1.29**	**<0.001***

The data is displayed as Mean ± SD. or frequency (%).

Table (3): Impact of sex difference on diabetic cardiac complications, cerebrovascular complications, microvascular complications, and PAD:

			Males (n=500)	Females (n=500)	P value
Cardiac complications					
	Dysrhythmia		**152 (30.4%)**	**115 (23%)**	**0.008***
Heart failure	**Preserved**		**38 (7.6%)**	**46 (9.2%)**	**0.892**
	Reduced		**20 (4%)**	**23 (4.6%)**	
	Chronic stable angina		**120 (24%)**	**119 (23.8%)**	**0.190**
IHD	**Acute coronary syndrome**	**Un stable angina**	**31 (6.2%)**	**30 (6%)**	
		Acute MI	**22 (4.4%)**	**37 (7.4%)**	
		CABG	**25 (5%)**	**29 (5.8%)**	
Cerebrovascular complications					
Stroke	**Ischemic stroke**		**86 (17.2%)**	**66 (13.2%)**	**0.178**
	Hemorrhagic stroke		**72 (14.4%)**	**34 (6.8%)**	
	TIA		**32 (6.4%)**	**22 (4.4%)**	**0.786**
Microvascular complications					
	Retinopathy		**107 (21.4%)**	**117 (23.4%)**	**0.448**
	CKD		**323 (64.6%)**	**256 (51.2%)**	**<0.001***
	Peripheral neuropathy		**236 (47.2%)**	**180 (36%)**	**<0.001***
PAD					
PAD	**Asymptomatic**		**183 (36.6%)**	**155 (31%)**	**0.061**
	ABI		**0.9 ± 0.26**	**0.91 ± 0.31**	**0.467**

Data is presented as Mean ± SD or frequency (%). * Myocardial Infarction(MI), Ankle Brachial Index (ABI), peripheral arterial disease (PAD). Ischemic heart disease (IHD). Coronary artery bypass graft (CABG). Chronic kidney disease (CKD).

Table (4): Impact of sex on compliance of drugs:

	Males (n=500) (%)	Females (n=500) (%)	P value
Anti-diabetic	**253 (50.6%)**	**234 (46.8%)**	**0.229**
Anti- ischemic	**201 (40.2%)**	**215 (43%)**	**0.369**
Anti- failure	**192 (38.4%)**	**202 (40.4%)**	**0.518**
Hypolipidemic	**228 (45.6%)**	**213 (42.6%)**	**0.339**

Table (5): Impact of sex differences Lifestyle:

		Males (n=500)	Females (n=500)	P value
Diet	**Unhealthy**	**49 (9.8%)**	**74 (14.8%)**	**0.035***
	Less healthy	**136 (27.2%)**	**141 (28.2%)**	
	Healthy	**315 (63%)**	**285 (57%)**	
Physical activity	**Sedentary**	**93 (18.6%)**	**99 (19.8%)**	**0.752**
	Mild	**259 (51.8%)**	**249 (49.8%)**	
	Moderate	**118 (23.6%)**	**127 (25.4%)**	
	Active	**28 (5.6%)**	**23 (4.6%)**	
Quality of life	**Poor**	**70 (14%)**	**93 (18.6%)**	**0.131**
	Fair	**148 (29.6%)**	**146 (29.2%)**	
	Good	**282 (56.4%)**	**261 (52.2%)**	

Data is displayed as frequency (%).

Discussion

The main causes of morbidity and death in diabetes patients who have a higher risk of heart failure, coronary artery disease (CAD), myocardial infarction (MI), diabetic cardiomyopathy (DCM), and stroke continue to be CVD problems [8]. SBP and DBP did not differ statistically between the two groups, according to our study showed that the effects of increasing SBP (every 10-mmHg rise) on CVD outcomes were comparable in both sexes [9]. Also, studies revealed that there is no sex-related variation in the stroke risk brought on by elevated DBP or SBP [10, 11]. This is inconsistent with a previous trial who discovered that men have a significantly greater chance of stroke occurrences than women when their DBP is elevated[12]. A previous trial discovered that women have a higher estimated national control of hypertension and hyperglycemia than males do[13]. A previous trial revealed that women have a far higher prevalence of SBP than men do[14].

In this research, it was observed that females exhibited notably higher BMI compared to males, with a recorded P value below 0.05. Conversely, females displayed a significantly lower waist circumference than males, also with a P value below 0.05. Studies discovered a higher prevalence of obesity among women with diabetes compared to men[15, 16]. A previous study [17] revealed that until reaching the eighth decade of life, women diagnosed with type 2 diabetes tend to have a higher BMI than men. A previous study [18] reported an average BMI for women at the time of type 2 diabetes diagnosis that is 1.8 kg/m2 greater than that of men after adjusting for age. Previous research proposed that variations in body size and distribution between genders might contribute to this observed difference [11]. The current study indicated a significantly lower prevalence of smoking in females compared to males, with a P value below 0.001. A previous study demonstrated that smoking increased the risk of coronary heart disease by 25% in women compared to men [9]. Additionally, levels of TC, HDL-C, LDL-C, and TG were notably higher in female subjects compared to males in this study, with a P value below 0.05.

According to previous studies, women with diabetes remain less likely to meet their goals for high-density lipoprotein cholesterol [15, 16]. According to previous study, there was no distinction in gender in the continuous log-linear relationships between BMI, blood pressure, and total cholesterol and the mortality from CHD or stroke[19]. These associations were also equivalent in strength across individuals with and without diabetes. In the NHANES, a previous study [20] discovered that diabetic women were less often on target for blood pressure, LDL-C, and HDL-C but not for HbA1c, TG, or non-HDL-C. According to a previous study [14], females have a much higher prevalence of LDL-C values than males. Age differences between genders in this study are statistically significant (P value <0.05). According to previous trial [21], the average age of a person in Italy was 56 years for males and 58 years for women. This contradicts the findings of previous study [22], who found a negligible variation in the mean age of presentation between the sexes. Additionally, previous trial discovered that there is a statistically

insignificant difference (P < 0.504) in the mean ages of the two sexes[23]. In people aged 20 to 49, previous study [24] found no significant variations in the prevalence or incidence of type 2 diabetes based on a person's gender. Furthermore, according to previous study there were significant differences in the prevalence of diabetes between people aged 50 and 59[25]. However, by the time people reached their seventh decade of life, there were no longer any significant sex differences, nor were there any between people aged 40 and 49 or between people aged 30 and 39. According to our research, females with diabetes have a substantially longer duration than males (P value <0.001). There is a negligible difference in the DM family history between the two groups. Each male and girl had a different type of diabetes, all of them type II. However, previous study discovered no discernible variation in the length of the disease between the male and female groups[22].

The current investigation revealed that males had significantly better healthy diet compliance than females. There is little variation in physical activity between the two groups. According to a previous study, baseline risk factor analysis showed that women were more physically inactive than men[26].

In previous study noted that the majority of participants expressed overall contentment with their quality of life[27]. However, they identified a strong link between poorer physical and mental health and the presence of diabetic issues alongside a higher HbA1c percentage. A previous study revealed that individuals with elevated-risk HbA1c (>8.6%) faced notably lower Health-Related Quality of Life (HRQoL) across various aspects [28]. Our study highlighted a significantly higher occurrence of peripheral neuropathy and CKD among men compared to women. Women experienced notably fewer instances of dysrhythmia than men. No significant statistical differences were found between the two groups concerning heart failure, acute coronary syndrome, stroke, transient ischemic attack, or retinopathy. A previous study [12] reported a higher incidence of stroke among men compared to women. However, our findings diverged from those of research, who found that while women had a higher diabetes-related excess risk of myocardial infarction than men, there was not a similar trend for heart failure or stroke[29]. A previous research indicated that the risk of incident CHD doubles in men and triples in women with diabetes compared to women without the condition[30].

According to previous research , women with T2D had a relative risk of stroke that was nearly 25% higher than that of men [11]. However, diabetes seems to be a bigger risk factor for CHD, CVD, and all-cause mortality in women than in males, according to previous research [31]. Notably, women with diabetes had a 57% increased risk of coronary heart disease (CHD) compared to men with the same condition. Furthermore, a previous trial discovered that while men and women have similar overall extra risks, those with type 2 diabetes have nearly a threefold higher risk of heart failure[32]. Furthermore, they found no gender disparity in the additional risk for stroke cases with T2D. There has been variability in the results of published studies about the impact of gender on the risk of stroke associated with diabetes; some have reported that women with diabetes have a higher risk than men with diabetes [33] a

similar risk [34] or a lower risk [35]. The prophylactic effect of female sex against CVD in women with diabetes is declining, according to an analysis that looked at biological and environmental factors. The authors emphasized the processes behind the diabetes-related endothelial degradation in females with diabetes. These mechanisms included the way that insulin and estrogen signaling interact, as well as how hyperglycemia affects estrogen receptor expression and activation. The subsequent proinflammatory environment accelerates the atherosclerotic process, which results in coronary artery disease, especially in women. Anti-diabetic, anti-ischemic, anti-failure, and hypolipidemic medications did not significantly differ between the two groups in our results. Studies have shown that women adhere to their medications less frequently than males do [36, 37]. Women do not necessarily benefit from medication adherence to the same degree that males do because of the well-established problems with women's underrepresentation in clinical [38]. According to a previous study diabetes-related sex variations in CVD may be made worse by gender and sex differences in treatment[39],. Despite their worse management of CVD risk factors, women's treatment intensities are comparable to or even lower than men's, according to previous trials [20, 40]. This is likely due to variations in national health systems and availability of care. According to previous trial[41], even when therapies were included as factors in the regression models, female gender still had a significant correlation with not meeting targets.

In this study, females exhibited notably lower fasting blood sugar levels than males. Conversely, women showed significantly higher HbA1c levels compared to men. A previous trial [42] highlighted a noteworthy difference in HbA1C between male and female patients. A previous trial reported that women diagnosed with type 2 diabetes had poorer control over blood pressure, cholesterol, and HbA1c levels compared to men[43]. However, a previous trial [44] did not find substantial evidence of a significant difference in HbA1C values between males and females. Conversely, a previous trial revealed that within the age range of 30-59 years, men exhibited significantly higher HbA1c levels than women ($P<0.05$) [45]. A previous study , on the other hand, observed minimal variation in HbA1c levels between male and female groups[22].

Limitations of the study:

As an observational study, persistent residual confounders persist despite attempts to control a wide range of predetermined confounding factors. Additionally, our reliance on self-reported data concerning smoking habits and medication usage, coupled with a limited number of occurrences for stroke subtypes, hampers the estimation of gender-specific relationships.

Conclusions:

Among Egyptian diabetic patients, Diabetes duration, family history of premature CVD, BMI, HbA 1C, and lipid profile were significantly higher in females than males. However, Waist circumference, smoking, and uric acid were significantly lower in females. Males with T2DM may be more susceptible to PN and nephropathy, whereas females with the same disease may have a lower

arrhythmia risk than men with the same disease.

References:

1. Schiebinger L, Klinge I, Sánchez de Madariaga I, Paik HY, Schraudner M, Stefanick M. Gendered innovations in science, health & medicine, engineering, and environment. Available at genderedinnovations stanford edu/what-is-gendered-innovations html Accessed January. 2011;21:2015.
2. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: A systematic analysis for the global burden of disease study 2013. Lancet. 2014;384:766-81.
3. Regitz-Zagrosek V, Oertelt-Prigione S, Prescott E, Franconi F, Gerdts E, Foryst-Ludwig A, et al. Gender in cardiovascular diseases: impact on clinical manifestations, management, and outcomes. Eur Heart J. 2016;37:24-34.
4. Annandale E, Riska E. New connections: Towards a gender-inclusive approach to women's and men's health. Curr Sociol. 2009;57:123-33.
5. Geary N. Counterpoint: physiologists should not distinguish "sex" and "gender". Am J Physiol Regul Integr Comp Physiol. 2010;298:2-4.
6. Giralt D, Domingues-Montanari S, Mendioroz M, Ortega L, Maisterra O, Perea-Gainza M, et al. The gender gap in stroke: a meta-analysis. Acta Neurol Scand. 2012;125:83-90.
7. Roger VL, Jacobsen SJ, Pellikka PA, Miller TD, Bailey KR, Gersh BJ. Prognostic value of treadmill exercise testing. Circulation 1998; 98:2836–2841
8. American Diabetes Association. (8) Cardiovascular disease and risk management. Diabetes Care. 2015;38:49-57. doi: 10.2337/dc15-S011. PMID: 25537708.
9. Peters SA, Huxley RR, Woodward M. Comparison of the sex-specific associations between systolic blood pressure and the risk of cardiovascular disease: a systematic review and meta-analysis of 124 cohort studies, including 1.2 million individuals. Stroke. 2013;4:2394-401.
10. Rapsomaniki E, Timmis A, George J, Pujades-Rodriguez M, Shah AD, Denaxas S, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. Lancet. 2014;383:1899-911.
11. Peters SAE, Carcel C, Millett ERC, Woodward M. Sex differences in the association between major risk factors and the risk of stroke in the UK Biobank cohort study. Neurology. 2020;95:2715-26.
12. Ramezankhani A, Parizadeh D, Azizi F, Hadaegh F. Sex differences in the association between diabetes and hypertension and the risk of stroke: cohort of the Tehran Lipid and Glucose Study. Biol Sex Differ. 2022;13:10.
13. Esteghamati A, Larijani B, Aghajani MH, Ghaemi F, Kermanchi J, Shahrami A, et al. Diabetes in iran: Prospective analysis from first nationwide diabetes report of national program for prevention and control of diabetes (nppcd-2016). Sci Rep. 2017;7:6-11.
14. Kajiwara A, Kita A, Saruwatari J, Miyazaki H, Kawata Y, Morita K, et al. Sex differences in the renal function decline of patients with type 2 diabetes. J Diabetes Res. 2016;2016:5-8.
15. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al. Executive summary: heart disease and stroke statistics--2013 update: a report from the American Heart Association. Circulation. 2013;127:143-52.
16. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the united states, 2011-2012. JAMA. 2014;3:806-14.
17. Logue J, Walker JJ, Colhoun HM, Leese GP, Lindsay RS, McKnight JA, et al. Do men develop type 2 diabetes at lower body mass indices than women? Diabetologia. 2011;54:3-6.
18. Paul S, Thomas G, Majeed A, Khunti K, Klein K. Women develop type 2 diabetes at a higher body mass index than men. Diabetologia. 2012;55:1556-7.
19. L G, WG H, J H. Sex-specific relevance of diabetes to occlusive vascular and other mortality: a collaborative meta-analysis of individual data from 980 793 adults from 68 prospective studies. Lancet Diabetes Endocrinol. 2018;6:538-46.

20. Ford ES. Trends in the risk for coronary heart disease among adults with diagnosed diabetes in the u.S.: Findings from the national health and nutrition examination survey, 1999-2008. Diabetes Care. 2011;34:37-43.
21. Aaberg ML, Burch DM, Hud ZR, Zacharias MP. Gender differences in the onset of diabetic neuropathy. J Diabetes Complications. 2008;22:83-7.
22. Abosrea M, Elmasry HA, Oraby MI. Gender differences in diabetic peripheral neuropathy. Egyptian Journal of Medical Research. 2020;1:55-64.
23. Javed A, Furqan A, Zaheer M, Kasuri N. Gender based differences in diabetic peripheral neuropathy. PJNS. 2014;9:20-4.
24. Lipscombe LL, Hux JE. Trends in diabetes prevalence, incidence, and mortality in Ontario, Canada 1995-2005: a population-based study. Lancet. 2007;369:750-6.
25. Choi YJ, Kim HC, Kim HM, Park SW, Kim J, Kim DJ. Prevalence and management of diabetes in korean adults: Korea national health and nutrition examination surveys 1998-2005. Diabetes Care. 2009;32:16-20.
26. Perreault L, Ma Y, Dagogo-Jack S, Horton E, Marrero D, Crandall J, et al. Sex differences in diabetes risk and the effect of intensive lifestyle modification in the diabetes prevention program. Diabetes Care. 2008;31:1416-21.
27. Al-Abadla Z, Elgzyri T, Moussa M. The Effect of Diabetes on Health-Related Quality of Life in Emirati Patients. Dubai Diabetes and Endocrinology Journal. 2022;28:35-44.
28. Svedbo Engström M, Leksell J, Johansson UB, Borg S, Palaszewski B, Franzén S, et al. Health-related quality of life and glycaemic control among adults with type 1 and type 2 diabetes - a nationwide cross-sectional study. Health Qual Life Outcomes. 2019;17:14-21.
29. Policardo L, Seghieri G, Francesconi P, Anichini R, Franconi F, Del Prato S. Gender difference in diabetes related excess risk of cardiovascular events: when does the 'risk window' open? J Diabetes Complications. 2017;31:74-9.
30. Peters SA, Huxley RR, Woodward M. Diabetes as risk factor for incident coronary heart disease in women compared with men: a systematic review and meta-analysis of 64 cohorts including 858,507 individuals and 28,203 coronary events. Diabetologia. 2014;57:1542-51.
31. Wang Y, O'Neil A, Jiao Y, Wang L, Huang J, Lan Y, et al. Sex differences in the association between diabetes and risk of cardiovascular disease, cancer, and all-cause and cause-specific mortality: a systematic review and meta-analysis of 5,162,654 participants. BMC Med. 2019;17:136.
32. Ballotari P, Venturelli F, Greci M, Giorgi Rossi P, Manicardi V. Sex Differences in the Effect of Type 2 Diabetes on Major Cardiovascular Diseases: Results from a Population-Based Study in Italy. Int J Endocrinol. 2017;2017:6039356.
33. Cui R, Iso H, Yamagishi K, Saito I, Kokubo Y, Inoue M, et al. Diabetes mellitus and risk of stroke and its subtypes among Japanese: the Japan public health center study. Stroke. 2011;42:2611-4.
34. Tanizaki Y, Kiyohara Y, Kato I, Iwamoto H, Nakayama K, Shinohara N, et al. Incidence and risk factors for subtypes of cerebral infarction in a general population: the Hisayama study. Stroke. 2000;31:2616-22.
35. Doi Y, Ninomiya T, Hata J, Fukuhara M, Yonemoto K, Iwase M, et al. Impact of glucose tolerance status on development of ischemic stroke and coronary heart disease in a general Japanese population: the Hisayama study. Stroke. 2010;41:203-9.
36. Krämer HU, Raum E, Rüter G, Schöttker B, Rothenbacher D, Rosemann T, et al. Gender disparities in diabetes and coronary heart disease medication among patients with type 2 diabetes: results from the DIANA study. Cardiovasc Diabetol. 2012;11:88-95.
37. Manteuffel M, Williams S, Chen W, Verbrugge RR, Pittman DG, Steinkellner A. Influence of patient sex and gender on medication use, adherence, and prescribing alignment with guidelines. J Womens Health 2014;23:112-9.
38. Regensteiner JG, Golden S, Huebschmann AG, Barrett-Connor E, Chang AY, Chyun D, et al. Sex differences in the cardiovascular consequences of diabetes mellitus: A scientific statement from the american heart association. Circ. 2015;132:2424-47.
39. Cenko E, Yoon J, Kedev S, Stankovic G, Vasiljevic Z, Krljanac G, et al. Sex Differences in Outcomes After STEMI: Effect

Modification by Treatment Strategy and Age. JAMA Intern Med. 2018;178:632-9.
40. Kautzky-Willer A, Kamyar MR, Gerhat D, Handisurya A, Stemer G, Hudson S, et al. Sex-specific differences in metabolic control, cardiovascular risk, and interventions in patients with type 2 diabetes mellitus. Gend Med. 2010;7:571-83.
41. Penno G, Solini A, Bonora E, Fondelli C, Orsi E, Zerbini G, et al. Gender differences in cardiovascular disease risk factors, treatments and complications in patients with type 2 diabetes: The riace italian multicentre study. J Intern Med. 2013;274:176-91.
42. Abudawood M, Tabassum H, Ansar S, Almosa K, Sobki S, Ali MN, et al. Assessment of gender-related differences in vitamin D levels and cardiovascular risk factors in Saudi patients with type 2 diabetes mellitus. Saudi J Biol Sci. 2018;25:31-6.
43. Wright AK, Kontopantelis E, Emsley R, Buchan I, Mamas MA, Sattar N, et al. Cardiovascular risk and risk factor management in type 2 diabetes mellitus: A population-based cohort study assessing sex disparities. Circ. 2019;139:2742-53.
44. Khan HA, Sobki SH, Khan SA. Association between glycaemic control and serum lipids profile in type 2 diabetic patients: HbA1c predicts dyslipidaemia. Clin Exp Med. 2007;7:24-9.
45. Ma Q, Liu H, Xiang G, Shan W, Xing W. Association between glycated hemoglobin A1c levels with age and gender in chinese adults with no prior diagnosis of diabetes mellitus. Biomed Rep. 2016;4:737-40.

To cite this article: Amira M. El Sayed, Walaa M. Ibrahim, Ayman M. Elbadawy, Sally H. Mohammed, Rasha O. Abd ElMoneim. Impact of Sex and Gender Differences on Cardiovascular Risk Factors and Cardiovascular Complications in Diabetic Patients in Benha City, Egypt: A Hospital-Based Cross-Sectional Study. BMFJ 2024;41(1):130-140.