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Research Article

Impact of Gender on Type II Diabetes Glycemic and Cardiovascular Markers Control and Treatment

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Abstract

Background and Objective: Type II Diabetes (T2D) is considered a major health burden locally, regionally and internationally. Gender differences in T2D prevalence were found in several epidemiological and observational studies. The primary goal of this study was to assess the prevalence of T2D-related comorbidities and treatment modalities and the impact of gender. **Materials and Methods:** This was a cross-sectional study that was conducted between June of 2013 and July of 2016 for patients with T2D at the 2 main outpatient diabetes clinics in Taif city, Saudi Arabia. Those with type I diabetes, gestational diabetes and drug-induced diabetes were excluded. **Result:** A total of 945 patients with a mean age of 58.4 ± 11.8 years with a nearly equal distribution among both genders but with slightly more male predominance (52.2%). When compared to females, male patients were more likely to be older ($p < 0.001$) and exhibit a longer T2D duration ($P 0.003$), lower mean BMI ($p < 0.001$), lower systolic blood pressure ($P 0.062$), higher diastolic blood pressure ($P 0.468$), less likely to have hypertension and be on ACE/ARB blockers ($P 0.065$ and 0.019 , respectively), more likely to have hyperlipidemia and be on a statin ($P 0.065$ and 0.124 , respectively), and more likely to have cardiac disease and stroke and to be on beta-blockers ($P 0.005$, 0.279 , 0.005 , respectively). **Conclusion:** Both genders exhibited comparable HbA1c levels. Medical treatment optimization along with controlling both measured cardiovascular makers and laboratory result levels was based on comorbidities and complications rather than gender.

Key words: Type 2 Diabetes, T2D, gender, cardiovascular, glycemic

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Type II Diabetes (T2D) is considered a major health burden locally, regionally and internationally. A recent nationwide study from Saudi Arabia showed that one-quarter of the included adults aged 30 years or older had T2D, and 40.3% of them were unaware of their disease¹. More recently, Saudi Arabia was ranked number two in the Gulf region regarding the highest prevalence of T2D after Bahrain². After the Caribbean region, the Middle East and North African regions have the second-highest diabetes prevalence worldwide³. Also, the prevalence of diabetes is expected to increase by more than 50% in the USA alone by 2030, according to a recent review⁴.

Gender differences in T2D prevalence were found in several epidemiological and observational studies. For example, a previous study in Saudi Arabia showed a higher prevalence of T2D among male individuals when compared to females⁵. This same study found that T2D was more prevalent in females when stratified by the age of 50 years and younger. Another more recent meta-analysis confirmed the female predominance regarding diabetes prevalence in Saudi Arabia⁶, while another study suggested the opposite with a higher male predominance regarding T2D prevalence globally⁷. This observed variation across studies is likely related to lifestyle, hormonal, socio-economical and environmental factors^{8,9}.

A cross-sectional study in Saudi Arabia showed that males were more likely to have larger waist circumferences and higher measured weights than females¹⁰. A recent study in Saudi Arabia showed that hypertension and prehypertension were more prevalent in male patients when compared to females and was correlated with weight and socioeconomic status¹¹. Males were more likely to have increased cardiovascular disease incidence that was associated with high cholesterol levels, while female cardiovascular disease incidence was associated with a higher blood pressure level¹². Males were more likely to suffer from a stroke when compared to females, with age being the most important risk factor¹³. A study conducted in the United Kingdom showed that females were less likely to smoke and that if they did, they smoked fewer cigarettes per day compared to males¹⁴. Sugar-sweetened beverages and fruit juice consumption was more common in male individuals according to a recent study¹⁵.

The primary goal of this study was to assess the prevalence of T2D-related comorbidities and complications among randomly selected T2D patients. This study will also evaluate the treatment modalities and its impact on disease control as well as the impact of gender.

MATERIALS AND METHODS

Study area: This was a cross-sectional study that was conducted between June of 2013 and July of 2016 for patients with T2D at the 2 main outpatient diabetes clinics in Taif city, Saudi Arabia. Adult T2D patients who agreed to participate were included in the study, while those with type I diabetes, gestational diabetes and drug-induced diabetes were excluded.

Data collection: The researcher collected baseline characteristics, including personal information, social data, educational achievement, smoking-related data and physical activity data from the patients. Data regarding comorbid conditions, diabetes duration, diabetes-related complications and diabetes-related medications were collected from the medical electronic records. It categorized the patient's economic status according to the reported monthly income, considering those with a monthly income of less than five thousand Saudi riyals as low income, while those with an income of fifteen thousand or more were characterized as high income. Severe hypoglycemia was defined as having blood glucose levels less than 55 mg dL⁻¹ in the last year and requiring other people's help in recovering from such an episode.

Clinical measurements: At the time of the clinical visit, the researcher reviewed the recent laboratory data from the same visitor within the previous 6 months from the evaluation date. It used the Modification of Diet in Renal Disease (MDRD) formula to calculate the Glomerular Filtration Rate (GFR)¹⁶. The researcher also collected data regarding the vital signs, height and weight that were measured by the nurse at the time of the visit. Subsequently, the Researcher calculated body mass index (BMI) values according to the universal standard definition.

Statistical analysis: All the data were initially entered into an Excel spreadsheet and then exported to Statistical Package for the Social Sciences (SPSS) software version 21. Each variable was expressed as frequency and percentage. The researcher used the T-test to compare between the means and the Chi-square test to assess the relationship between the variables. The researcher compared the group based on the gender of the patients.

RESULTS

Baseline characteristics: A total of 945 patients with a mean age of 58.4±11.8 years with 47.8% of them were male

(Table 1). The mean diabetes duration was 12.7 ± 8.6 years and mean BMI of 32.1 ± 6.1 (Kg m^{-2}). The mean systolic and diastolic blood pressure were 135.7 ± 21.5 and 77.0 ± 11.6 , respectively. Most of the patients were married and reported low levels of educational achievements with 57.5% of them reported low income. Hyperlipidemia was the most reported comorbidities followed by hypertension. Neuropathy followed by retinopathy were the most common diabetes-related complications. Most of the patients were on a combined oral hypoglycemic and insulin regimen. Metformin was the most prescribed oral medication followed by sulfonylurea, while thiazolidinediones (TZDs) were the least commonly prescribed oral medications. Statin was prescribed for 74.4% of patients, while ACE inhibitors/ARB blockers were prescribed 45.3% of the patients. The mean HbA1c was uncontrolled ($8.8 \pm 2.0\%$), while the lipid panel was controlled for an average risk T2D patient. Most of the patients had stage 1 chronic kidney disease according to the average calculated GFR. Most of the patients reported a sedentary lifestyle, and 27.4% of them reported an activity level below recommended levels of physical activity for T2D patients. Around 10% of the patients were active smokers, while one-fourth were passive smokers. Baseline characteristics based on the gender of the patients: overall, 52.2% of the patients were male (Table 2). When compared to females, male patients were more likely to be older ($p < 0.001$) and exhibit a longer T2D duration ($P 0.003$), lower mean BMI ($p < 0.001$), lower systolic blood pressure (p -value 0.062) and higher diastolic blood pressure (p -value 0.468). Males were also more likely to be married ($p < 0.001$), have a higher educational level ($p < 0.001$) and be less likely to report lower income ($p < 0.001$), less likely to have hypertension and be on ACE/ARB blockers ($P 0.065$ and 0.019 respectively), more likely to have hyperlipidemia and be on a statin (p -value 0.065 and 0.124 , respectively), have lower total cholesterol and HDL levels but higher triglyceride ($P 0.096$, < 0.001 and 0.002 , respectively), be less likely to report severe hypoglycemia but more likely to be on insulin agents and less likely to be on a sulfonylurea (p -value 0.002, 0.403 and 0.263 respectively). Males were also more likely to have cardiac disease and stroke and to be on beta-blockers (p -value 0.005, 0.279 , 0.005 , respectively). They were more likely to have retinopathy ($P 0.001$) and less likely to have neuropathy and renal failure (p -value 0.410 and 0.138 , respectively). Males also had lower GFR levels and were less likely to be on metformin ($p < 0.001$ and 0.278 , respectively) and more likely to be on DPP-4 inhibitors and TZDs (p -value 0.114 and 0.016 respectively). Males had comparable HbA1c levels to females

Table 1: Baseline characteristics of the whole cohort

Baseline characteristics (N = 945)	
Mean age (years)	58.4 ± 11.8
Male (%)	47.8
Mean diabetes duration (years)	12.7 ± 8.6
Mean BMI (Kg m^{-2})	32.1 ± 6.1
Mean systolic blood pressure (mmHg)	135.7 ± 21.5
Mean diastolic blood pressure (mmHg)	77.0 ± 11.6
Socioeconomic (%)	
Single	4.1
Divorced	3.3
High school or less	87.2
Bachelor's degree or higher	12.8
Low income	57.5
High income	5.9
Comorbidities and complications (%)	
Hypertension	54.0
Hyperlipidemia	76.0
Sever hypoglycemia	31.3
Retinopathy	38.9
Neuropathy	61.9
Renal failure	4.2
Cardiac disease	20.0
Stroke	6.3
Medications (%)	
Metformin	78.9
Sulfonylurea	31.9
Dipeptidyl peptidase inhibitors (DPP-4 inhibitors)	17.1
Thiazolidinediones (TZDs)	1.4
Insulin alone	15.4
Oral hypoglycemic agents and insulin	47.0
Oral hypoglycemic agents alone	35.8
Angiotensin converting enzyme inhibitors/Angiotensin Receptor Blockade	45.3
Beta-blockers	4.0
Statin	74.4
Laboratory data	
HbA1c (%)	8.8 ± 2.0
Total cholesterol (mmol L^{-1})	4.2 ± 2.0
Low density lipoprotein (LDL) (mmol L^{-1})	2.4 ± 1.1
High density lipoprotein (HDL) (mmol L^{-1})	1.0 ± 0.4
Triglyceride (mmol L^{-1})	1.6 ± 1.0
Creatinine (mmol L^{-1})	85.8 ± 59.3
Calculated Glomerular Filtration Rate (GFR) (mL/min/1.73 m^2)	94.1 ± 41.5
Lifestyle habits	
Sedentary lifestyle (%)	59.2
Exercise <150 min/week	27.4
Exercise 150-300 min/week	9.3
Exercise >300 min/week	4.1
Active smoking (%)	9.8
Passive smoking (%)	25.5

(p -value 0.701) but were more likely to be physically active and active smokers (both $p < 0.001$) and were less likely to be passive smokers (p -value 0.105).

When researchers compared genders based on achieving the glycemic and cardiovascular goals stated by the American

Table 2: Baseline characteristics based on the gender of the patients

Characteristics	Male	Female	p-value
Percent of patients	52.2	47.8	n/a
Mean age (years)	60.1±12.1	56.5±11.3	<0.001
Mean diabetes duration (years)	13.6±8.8	11.9±8.4	0.003
Mean BMI (Kg m ⁻²)	30.5±5.4	33.9±6.3	<0.001
Mean systolic blood pressure (mmHg)	134.4±20.2	137.1±22.8	0.062
Mean diastolic blood pressure (mmHg)	77.2±12.1	76.7±11.1	0.468
Socioeconomic (%)			
Single	2.6	5.8	<0.001
Divorced	0.8	6.0	
High school or less	81.7	93.1	<0.001
Bachelor's degree or higher	18.3	6.9	
Low income	42.8	73.5	<0.001
High income	8.7	2.9	
Comorbidities and complications (%)			
Hypertension	51.5	56.6	0.065
Hyperlipidemia	78.1	73.7	0.065
Sever hypoglycemia	27.0	36.1	0.002
Retinopathy	43.6	33.8	0.001
Neuropathy	61.5	62.4	0.410
Renal failure	3.4	5.1	0.138
Cardiac disease	23.3	16.4	0.005
Stroke	6.9	5.8	0.279
Medications (%)			
Metformin	78.1	79.9	0.278
Sulfonylurea	30.8	33.0	0.263
Dipeptidyl peptidase inhibitors (DPP-4 inhibitors)	18.7	15.5	0.114
Thiazolidinediones (TZDs)	2.2	0.4	0.016
Insulin alone	15.9	14.9	0.403
Oral hypoglycemic agents and insulin	48.9	44.9	
Oral hypoglycemic agents alone	33.8	38.0	
Angiotensin converting enzyme inhibitors/Angiotensin Receptor Blockade	42.0	48.9	0.019
Beta-blockers	5.7	2.2	0.005
Statin	76.1	72.6	0.124
Laboratory data			
HbA1c (%)	8.8±2.0	8.8±2.0	0.701
Total cholesterol (mmol L ⁻¹)	4.1±1.5	4.3±1.0	0.096
Low density lipoprotein (LDL) (mmol L ⁻¹)	2.4±1.1	2.4±1.1	0.644
High density lipoprotein (HDL) (mmol L ⁻¹)	0.9±0.4	1.0±0.5	<0.001
Triglyceride (mmol L ⁻¹)	1.7±1.1	1.5±1.0	0.002
Creatinine (mmol L ⁻¹)	97.3±59.2	73.3±56.9	<0.001
Calculated Glomerular Filtration Rate (GFR) (mL/min/1.73 m ²)	87.0±34.9	101.8±46.5	<0.001
Lifestyle habits			
Sedentary lifestyle (%)	51.7	67.3	<0.001
Exercise <150 min/week	32.3	22.1	
Exercise 150-300 min/week	9.1	9.5	
Exercise >300 min/week	6.9	1.1	
Active smoking (%)	17.6	1.8	<0.001
Passive smoking (%)	23.2	27.9	0.105

Diabetes Associations for average-risk patients, the researcher observed no statistically significant difference between the groups (Fig. 1).

The partial correlation calculated while adjusting for age, marital status, income, educational status, BMI, duration of T2D diagnosis, exercise, active and passive smoking, HbA1c level, lipid profile, systolic blood pressure,

hypertension, hyperlipidemia and micro- and macrovascular complications showed a significant negative correlation between genders and ACE/ARB inhibitors use ($r = -0.115$, $P 0.005$) and non-significant positive correlations between gender and both metformin use ($r = 0.006$, p -value 0.894) as well as statin use ($r = 0.025$, p -value 0.552).

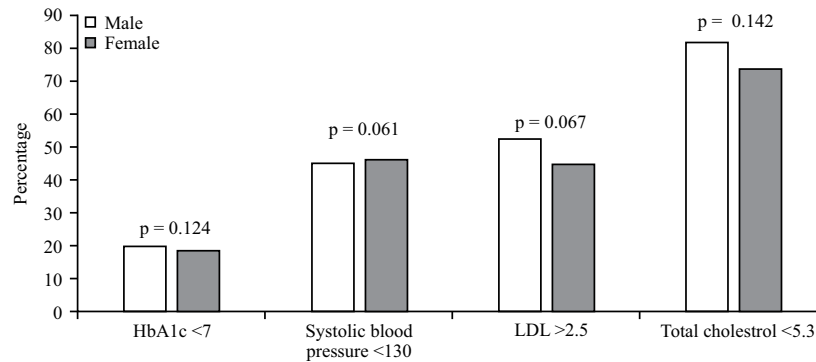


Fig. 1: Achievements of cardiovascular/glycemic goals in T2D patients based on gender

DISCUSSION

This study showed that male patients tended to be older with a longer duration of T2D but with lower BMI and systolic blood pressure. This is consistent with previous study findings that showed that females tended to have higher BMI values at the time of the diagnosis and that BMI was inversely related to age¹⁷. This may be explained by the increased insulin resistance in male patients compared to females at the same BMI, which is due to hormonal differences as well as the excess visceral and hepatic fat in male patients¹⁸.

Also, in this study male patients were more likely to be married and have a better educational level and monthly income. A previous study showed that T2D prevalence increased among those with lower educational levels¹⁹. Low income has also been shown to be associated with increased T2D prevalence²⁰. A recent study showed a correlation between marital status and mortality, with single males having a high mortality rate, while widowed/divorced females with low educational levels had higher mortality rates²¹.

Hyperlipidemia, stroke and cardiac disease were more common in this study of male patients. One previous study showed that females were more likely to suffer from a stroke from an interaction between T2D and hypertension²². The discrepancy between the former study and the study finding is likely because the study female patients were less likely to have hypertension. The observed high risk for cardiovascular disease is likely explained by older age, a higher rate of smoking and a higher risk of hypertension, as shown in previous studies^{23,24}.

This study showed that male patients were more likely to be on statin and beta-blockers because males were more likely to have a history of hyperlipidemia and cardiac disease. The statin uses found in this study are similar to what has been

reported in recent literature, and the observed gender differences were likely related to the comorbidities and the fact that this study male patients were older rather than the presence of gender bias^{25,26}. The ACE inhibitors/ARB were less likely to be prescribed for male patients in this study. A recent publication showed that males with T2D were significantly more likely to be prescribed ACE inhibitors²⁷. This study finding reflects no gender bias since the female patients were more likely to have hypertension and that may explain the difference that was observed.

This study showed comparable glycemic control and lipid control except for slightly better HDL levels in females. This is consistent with other study findings with excess risk of hypoglycemia in female patients²⁸. The severe hypoglycemia observed in study may be explained by sulfonylurea.

More females in this study reported a sedentary lifestyle when compared to male patients. A previous study showed that males were more likely to report higher physical activity than females²⁹. However, another previous study showed that patients for both genders were less likely to be physically active³⁰. This could be explained by the social and climatic differences that allowed this study patients to exercise. On a similar note, the prevalence of active smoking in this study is lower than what has been reported in a larger cohort³¹.

The sample size of the present study was small, but the sample does represent the T2D population in Taif city since the data were collected over a longer duration and from the 2 main diabetes outpatient centers.

CONCLUSION

Our male patients exhibited longer T2D durations, were older, and had higher educational and economic status than females. However, despite this, they exhibited comparable

HbA1c levels. Medical treatment optimization along with controlling both measured cardiovascular makers and laboratory result levels was based on comorbidities and complications rather than gender. The observed increased risk of severe hypoglycemia in females was likely related to sulfonyleurea and was potentially associated with the educational and economic status of the female patients rather than gender disparities.

SIGNIFICANCE STATEMENT

This study will expand the knowledge related to gender disparities reported previously in patients with diabetes. Despite the observed difference in the educational and socioeconomic levels between both gender, the study didn't observe any significant difference in glycemic control or treatment modalities. The treatment was directed to the health problem and unrelated to gender.

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