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Urinary bladder wall thickness in type 2 diabetes mellitus patients

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Keywords
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Abstract

Introduction: Diabetes mellitus is an increasing health challenge with accompanying urological complications. Over 50% of men and women with diabetes have bladder dysfunction. According to the current understanding of bladder dysfunction, it refers to a progressive condition encompassing a broad spectrum of lower urinary tract symptoms including urinary urgency, frequency, nocturia, and incontinence. Urinary bladder dysfunction has been classically described as diminished bladder sensation, poor contractility, and increased post-void residual urine, termed bladder cystopathy. Ultrasonography of the urinary bladder, which is a cheap, safe, radiation free, non-invasive and reliable imaging modality, may help to identify diabetes mellitus patients prone to develop urinary bladder dysfunction. **Method:** The study population comprised 80 diabetic subjects recruited from the diabetic outpatient clinic and another 80 age- and sex-matched asymptomatic control subjects. Ultrasound scan of their urinary bladder wall was performed using a curvilinear transducer to determine the thickness and other sonographic features. **Results:** Out of the 80 diabetic subjects, 30 (37.5%) were males, while 50 (62.5%) were females; of 80 non-diabetic control subjects, 40 (50%) were males and 40 (50%) were females. The mean age of the diabetic subjects was 59.5 ± 10.4 years with a range of 40–82 years, while that of the controls was 60.2 ± 7.4 years with a range of 40–85 years. There was no statistically significant difference ($p = 0.637$) between the mean age of the diabetic and control subjects. The mean urinary bladder wall thickness in the diabetics was greater than in the non-diabetics in the study subjects. There was a statistically significant difference between the urinary bladder thickness of diabetic subjects and the control group ($p < 0.001$). The mean urinary bladder wall thickness of the male and female subjects included in this study was 2.84 ± 1.31 mm and 2.9 ± 1.37 mm, respectively, with no statistically significant difference between them ($p = 0.159$). It was statistically significant between diabetic men and women ($p = 0.027$). Using Spearman's rank correlation to test the relationship between the glycaemic haemoglobin level of diabetic subjects and urinary bladder wall thickness, it was revealed that there was no correlation between these variables (Spearman's rho = 0.119, $p = 0.309$). The relationship between the urinary bladder volume of diabetic subjects and their mean urinary bladder wall thickness showed no correlation either (Spearman's rho = –0.009, $p = 0.937$). Only gender was a statistically significant predictor of urinary bladder wall thickness among other variables. Conclusion: Mean bladder wall thickness in patients with type 2 diabetes mellitus was greater than in the control subjects, and also greater in diabetic men compared to diabetic women, but the difference did not attain statistical significance. Urinary bladder wall thickness of the diabetics did not correlate with their glycaemic haemoglobin levels. Only gender was found to be a predictor of bladder wall thickness.

Introduction

Diabetes mellitus is an endocrine disease that affects many people across the world. Diabetes mellitus, also called diabetes, is a long-standing condition that occurs when there are elevated levels of sugar in the blood circulation because the pancreas cannot produce any or enough of the hormone insulin or use insulin effectively[1]. Insulin is an essential hormone produced in the pancreas, and it aids in the uptake of glucose in the bloodstream into the body cells where glucose is converted into energy. The inability of the body cells to respond to insulin or lack of insulin leads to elevated levels of blood glucose, or hyperglycaemia, which is a special mark of diabetes.

Hyperglycaemia, if left unchecked over the long term, can cause damage to various body organs, leading to the development of disabling and life-threatening complications such as cardiovascular disease, neuropathy, nephropathy and eye disease, leading to retinopathy and blindness. However, if an appropriate treatment of diabetes is initiated, these serious complications can be delayed or averted.

The classification and diagnosis of diabetes are complex and have been the subject of much consultation, debate and revision stretching over many decades, but it is now widely accepted that there are three main types of diabetes: type 1 diabetes, type 2 diabetes and gestational diabetes (GDM).

Some less common types of diabetes also exist which include monogenic diabetes and secondary diabetes. Monogenic diabetes is caused by a single genetic alteration in an autosomal dominant gene rather than the contributions of many genes and environmental factors as seen in type 1 and type 2 diabetes. Examples of monogenic diabetes include conditions like maturity-onset diabetes of the young (MODY) and neonatal diabetes mellitus. Around 1–5% of all diabetes cases are due to monogenic diabetes[2–7]. Secondary diabetes arises as a complication of other diseases such as hormone disturbances (e.g. Cushing's disease or acromegaly), pancreatic diseases (for example, pancreatitis) or due to medications (e.g. corticosteroids).

The incidence of diabetes is increasing at a fast rate, with an expected global incidence of not less than 640 million people by 2040. Four hundred and twenty five million people worldwide, or 8.8% of adults aged 20–79 years, are estimated to have diabetes, and about 79% of these live in low- and middle-income countries.

If the age range is expanded to 18–99 years, the number of people with diabetes increases to 451 million. Given the current trend, it is estimated that by 2045, 693 million people aged between 18 and 99 years, or 629 million of people aged between 20 and 79 years, will have diabetes.

The vast majority of persons with diabetes have type 2 diabetes, which occurs when insulin resistance is present in fat and muscle cells, hepatic glucose output is enhanced, and insulin secretion fails to compensate[8]. Genetic studies have identified more than 150 so-called risk alleles for type 2 diabetes-variations in genes that increase a person's susceptibility to diabetes[8]. Diabetes and urologic diseases are very common health problems that markedly grow in prevalence and incidence with increasing age[9–11]. Diabetes is seen with an earlier onset and increased severity of urologic diseases, resulting in costly and debilitating urinary system complications. Urologic complications, including bladder dysfunction, sexual and erectile dysfunction, as well as urinary tract infections (UTIs), have a great effect on the quality of life of men and women with diabetes[12]. Over half of men and women with diabetes develop urinary bladder dysfunction[13,14]. According to the current understanding of bladder dysfunction, it refers to a progressive condition encompassing a broad spectrum of lower urinary tract symptoms including urinary urgency, frequency, nocturia, and incontinence. Previously, the dysfunction has been classically described as diminished bladder sensation, poor contractility, and increased post-void residual urine, termed bladder cystopathy[15]. However, bladder cystopathy most likely represents end-stage bladder failure with symptoms of infrequent micturition, difficulty initiating voiding, and post-void fullness, and it is relatively uncommon[12].

A number of clinical studies in people with diabetes have reported bladder instability or hypersensitivity as the most common findings, ranging from 39–61% of subjects[14,16]. Diminished bladder contractility or sensation has been found less often[14], and a non-contractile bladder appears to be quite uncommon.

Evidence suggests an increased prevalence of urgency with or without urge urinary incontinence among women with type 2 diabetes[17] and an increasing trend with longer duration of diabetes[18]. Overactive bladder (OAB), a highly prevalent and disturbing disease, is also based on the symptoms of urgency, with or without urge urinary incontinence, usually with frequency and nocturia[19]. Although urodynamic studies are widely used in patients with symptoms of OAB, only 54% show detrusor overactivity on conventional urodynamics[20]. Similarly, 55% of diabetic patients with OAB and 25% of asymptomatic patients with diabetes show detrusor overactivity during urodynamic studies[14,21].

Bladder wall thickness has been shown to be significantly increased in women with detrusor overactivity[22]. This variable has also been applied in the assessment of voiding dysfunction, bladder outlet obstruction, and as a screening tool in the assessment of upper urinary tract deterioration in children with myelodysplasia[23,24]. This is why urinary bladder dysfunction is to be assessed in type 2 diabetes mellitus by measuring the urinary bladder wall thickness using sonography in this study. Bladder wall hypertrophy is caused by the thickening of the detrusor[25]. It was hypothesised that detrusor wall thickness (DWT) or bladder wall thickness (BWT) reflects the workload of the bladder similar to the heart, whereby the cardiac wall thickens due to arterial hypertension or cardiac valve stenosis[26]. In animal studies, diabetes has been shown to result in hypertrophy of the bladder wall with an increase in smooth muscle and urothelium thickness[27]. Diabetes mellitus patients with OAB may also have an increased risk for bladder wall thickness, which may have a prognostic potential.

Ultrasound is a fast, readily available, and inexpensive modality, and it does not produce a claustrophobic effect like MRI. Ultrasonography is effective in evaluating the urinary bladder wall thickness and it does not utilise ionizing radiation like cystography and abdominal computed tomography which can also be used to evaluate the urinary bladder. However, cystography cannot adequately assess the urinary bladder wall thickness, while CT is quite expensive.

The aim of this study is to evaluate the urinary bladder wall thickness in type 2 diabetes mellitus patients with or without overactive bladder syndrome. The findings will be correlated with the relevant clinical and laboratory parameters.

Material and method

This was a case-control cross-sectional study carried out at the Departments of Radiology of our institution.

Subject selection

The study was carried out in adult subjects with type 2 diabetes mellitus. They were recruited from the Diabetes Outpatient Clinic at our institution. The subjects included newly diagnosed diabetics and those on follow-up attending the clinic. The control group consisted of individuals with fasting blood glucose levels less than 6.1 mmol/l and with no known history of diabetes mellitus.

Written informed consent was obtained from both subjects and controls.

Inclusion and exclusion criteria

Inclusion criteria for cases

The subject group included individuals attending the Diabetes Outpatient Clinic of OAUTHC in Ile-Ife that are above 40 years of age, diagnosed with Type 2 diabetes mellitus by an endocrinologist based on the WHO 1997 criteria which include any of the following[28]:

- Fasting plasma glucose of 126 mg/dl (7.0 mmol/L) or higher on two separate tests.
- Symptoms of diabetes plus a random blood glucose of 200 mg/dl (11.1 mmol/L) or higher.
- Two-hour plasma glucose >200 mg/dl (11.1 mmol/L) during an oral glucose tolerance test.
- Glycated haemoglobin (HbA_{1c}) of >48 mmol/L (>6.5 DCCT Diabetes Control and Complications Trial %).

Exclusion criteria for cases

- History of urologic disease, for example urethral stricture, meatal narrowing, and posterior urethral valve.
- History of spinal cord operation or previous pelvic operation that might have injured the presacral nerve plexus, such as surgical correction of imperforate anus.
- Neurologic disease such as transverse myelitis, meningomyelocele, Parkinson's disease, multiple sclerosis, spinal cord injury or stroke.
- Urinary tract infection.
- Patients on medication that could affect bladder function, such as diuretics or calcium channel blockers.
- Patients who currently use or previously used antimuscarinics were also excluded to avoid a likely effect on bladder wall thickness.
- Women with evidence of significant pelvic lesion/mass or genital prolapse.
- Pregnancy.
- Patients with signs of bladder outlet obstruction; or with residual volume over 20 ml.
- Patients with obvious neurogenic disorders, stone disease, genitourinary malignancies and/or a history of lower urinary tract injury or surgery were excluded from the study.
- Persons who did not give their consent for whatever reason.

Inclusion criteria for the controls

- Healthy volunteers comprising hospital staff, patient relatives and individuals presenting to the Radiology Department for other investigations (e.g. routine medical check-up).
- Fasting blood glucose in the range of 4.0–5.6 mmol/L.
- No known history of DM.

Exclusion criteria for the controls

- Subjects who did not meet the inclusion criteria for the control group.
- Subjects with any exclusion criterion for cases.
- Persons who did not give their consent for whatever reason.

Equipment and materials

- Versana Essential real-time ultrasound machine: manufactured by GENERAL ELECTRICS® GE Medical Systems (China) Co. Ltd with Serial No. 6023098WX0, equipped with a 3.5–3.8 MHz curvilinear transducer.

Clinical assessment

A written consent was obtained from all study participants.

The following general information were collected and recorded: age, gender and date of diagnosis of diabetes (or duration of diabetes). Clinical history was obtained from DM subjects to know the duration of their illness (or age at diagnosis).

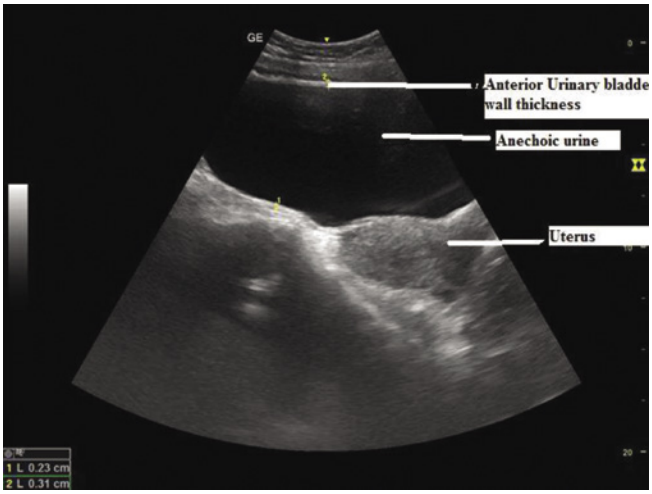

Fig. 1. *Sonographic image of the urinary bladder-longitudinal view showing the urinary bladder wall thickness in a female, with the uterus shown posterior to the urine distended urinary bladder*

Sonographic assessment technique

The patients were asked to drink an adequate volume of water until they felt a strong desire to void.

The bladder was moderately distended to stretch the wall and better visualise the mucosal surface and bladder lumen. Images were obtained in the transverse and longitudinal planes (Fig. 1)[29].

The bladder wall thickness (BWT) was measured from the interface of the anechoic urine and bladder mucosa to the outer part of the muscle layer. It was measured perpendicular to the luminal surface of the bladder in the anterior bladder wall. Estimated urinary bladder volume was obtained[30]. Post-void residual (PVR) urine was measured after toilet voiding. Wipes were used to clean off the gel from the examined areas upon completion of the examination.

Statistical analysis

Various parameters of the examination were recorded in the patient data sheet and entered into the computer spreadsheet using Statistical Package for Social Science (SPSS Inc., Chicago, IL, USA) software, version 20.0 (2016) for Windows.

Quantitative data for descriptive analysis were described in mean, median, standard deviation (SD), and minimum and maximum values, while categorical variables were summarised in simple and relative frequencies.

Independent t-test was applied to compare the means of the urinary bladder wall thickness of diabetic subjects with the control group.

The relationship between glycated haemoglobin levels and urinary bladder wall thickness was determined using Spearman's correlation coefficient. Spearman's rank correlation was also used to test the relationship between other continuous variables. Possible correlations between the urinary bladder wall thickness and gender, age, BMI, HBA_{1c}, FBG, and duration of diabetes mellitus were evaluated using multiple regression analysis.

The statistical level of confidence was set at ≤0.05, and the results were presented in tables and charts.

Results

Characteristics of study population

A total of 160 study subjects were recruited, comprising 80 adult subjects with diabetes mellitus aged 40 years and above; in order to ensure the exclusion of type 1 DM; and an equal number of age- and sex-matched apparently healthy controls.

Out of the 80 diabetic subjects, 30 (37.5%) were males, while 50 (62.5%) were females; of the 80 non-diabetic controls, 40 (50%) were males and 40 (50%) were females. There was no statistically significant difference in the numbers of males and females between the diabetic subjects and the control group (p = 0.111).

The mean age of the diabetic subjects was 59.5 ± 10.4 years (Tab. 1) with a range of 40–82 years, while that of the controls was 60.2 ± 7.4 years with a range of 40–85 years (p = 0.637). The majority of the diabetic subjects (41.25%) were aged between 60 years and 69 years, 21.25% were aged

Tab. 1. *Demographic characteristics of study subjects*

Variables	Diabetic *n* = 80	Non-diabetic *n* = 80	Statistics	Df	*p* value
Age (years)					
*Mean ± SD**	59.5 ± 10.4	60.2 ± 7.4	0.473	158	0.6368
(Range)	(40–82)	(42–85)			
*Male (mean ± SD)**	61.6 ± 8.4	60.1 ± 8.2	0.7606	68	0.4495
*Female (mean ± SD)**	58.2 ± 11.4	60.2 ± 6.5	1.0034	88	0.3184
***n* (%)**					
<50	15 (18.75)	7 (8.75)	0.473	158	0.6368
50–59	17 (21.25)	28 (35.0)			
60–69	33 (41.25)	37 (46.25)			
≥70	15 (18.75)	8 (10.0)			
Gender, *n* (%)**					
Male	30 (37.5)	40 (50.0)	2.5397	1	0.111
Female	50 (62.5)	40 (50.0)			
BMI					
*(Mean ± SD)**	27.06 ± 6.08	27.77 ± 4.39	0.8313	158	0.4071
Range	(17.58–39.84)	(18.69–37.37)			
Underweight	5 (6.25)	0 (0.0)	1.282	2	0.108
Normal	25 (31.25)	21 (26.25)			
Overweight	25 (31.25)	37 (46.25)			
Obese	25 (31.25)	22 (27.5)			

* Independent sample t-test was used to compare the means,
** chi square

Tab. 2. *Clinical parameters in type 2 diabetes mellitus patients*

Variables	Diabetic *n* = 80	Non-diabetic *n* = 80
FBG in mmol/L* *(Mean ± SD)*	7.6 ± 3.5	4.42 ± 0.4
(Range)	(3.3–21.3)	(2.4–4.5)
n (%)		
Good control (FBG <7.0)	47 (58.75)	
Poor control (FBG >7.0)	33 (41.25)	
HBA_{1c} in %*	7.0 ± 2.71	
(Range)	(4.0–15.0)	
n (%)		
Good control (HBA_{1c} <6.5)	44 (56.41)	
Poor control (HBA_{1c} >6.5)	34 (43.59)	

* Independent sample t-test was used to compare the means
# chi square test was used to compare the proportions
SD – standard deviation; BMI – body mass index; FBG – fasting blood glucose; HbA_{1c} – glycated haemoglobin

Tab. 3. *Comparison of urinary bladder wall thickness among diabetic and non-diabetic patients*

Urinary bladder wall thickness in mm *n* (%)		Study participant Mean ± SD *(range)*	*P* value
Diabetics	80 (50.0)	3.18 ± 1.50 *(1.68–4.68)*	**<0.001**
Non-diabetics	80 (50.0)	2.18 ± 0.41 *(1.77–2.59)*	

* Independent t-test was used to compare the means
SD – standard deviation

between 50 and 59 years, 18.75% were aged between 40 and 50 years, and 18.75% were aged 70 years and older. The majority of the control subjects (48.75%) were also aged between 60 and 69 years, similarly to the diabetic subjects, 35.0% were aged between 50 and 59 years, 7.50% were aged 60–69 years, while 8.75% were aged 70 years or more.

The mean height of the diabetic subjects was 1.63 ± 0.1 m, while that of controls was 1.58 ± 0.08 m. The range of height of the diabetic subjects was between 1.3 m and 1.9 m, while that of the control subjects was between 1.4 m and 1.8 m.

The mean weight of the diabetic subjects was 71.9 ± 14.5 kg and that of the controls was 69.1 ± 10.4 kg with a range of 40.5–108 kg for the diabetic subjects and 50–108 kg for the control subjects. There is, however, no statistical significant difference in the BMI between the diabetic and non-diabetic subjects of this study (p = 0.4071) (Tab. 1). The mean BMI of both the diabetic and non-diabetic study groups were 27.06 ± 6.08 kg/m² and 27.77 ± 4.39 kg/m², respectively. The highest number of patients were overweight both in the diabetic and non-diabetic groups. Only three out of the 80 diabetic subjects had urinary symptoms.

Blood glucose measurements of participants

Mean fasting blood glucose was 7.6 ± 3.5 mmol/L and 4.42 ± 0.4 mmol/L in the diabetic and control groups, respectively, with a range of 3.3–21.3 mmol/L and 2.4–4.5 mmol/L, respectively (Tab. 2). Forty-seven (58.75%) of them had good fasting blood glucose control (FBG <7.0 mmol/L) while 41.25% (33) had poor FBG (FBG >7.0 mmol/L). The mean fasting blood glucose in the control subjects was 4.42 ± 0.4 mmol/L.

The mean glycated haemoglobin level (HbA_{1c}) among the people with diabetes was 7.0 ± 2.7% (Tab. 2) with a range of 4–15%. 56.41% (44) of these subjects had good control (HBA_{1c} <6.5%), while 43.59% (34) had poor control (HBA_{1c} >6.5%). Three patients among the diabetics presented with urinary symptoms ranging from urgency, incomplete bladder emptying, frequency, nocturia, to difficulty initiating voiding. All of them were females with poor glycaemic control (9–11%).

Urinary bladder wall thickness ultrasound measurements

Comparison between the urinary bladder wall thickness in diabetics and non-diabetics

There was a statistically significant difference in the urinary bladder wall thickness between the diabetic subjects and the control group (p <0.001). The ranges of urinary bladder wall thickness in the diabetics and non-diabetics were 1.68–4.68 mm and 1.77–2.59 mm, respectively, with a mean of 3.18 ± 1.50 mm and 2.18 ± 0.41 mm, respectively (Tab. 3).

Comparison of gender with the urinary bladder wall thickness

The ranges of urinary bladder wall thickness among the men and women included in this study were 1.52–4.15 mm and

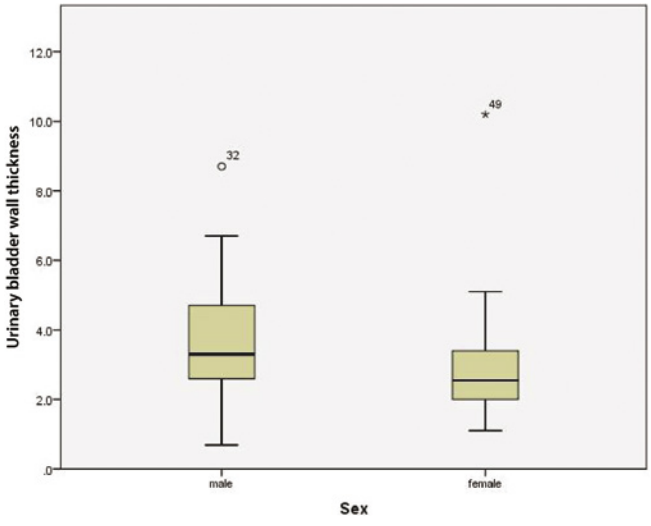

Fig. 2. *Box plot showing urinary bladder wall thickness in male and female patients*

Tab. 4. *Comparison of the urinary bladder wall thickness among all the study participants*

Urinary bladder wall thickness in mm *n* (%)		Study participant Mean ± SD *(range)*	*P* value
Male	70 (43.75)	2.84 ± 1.31 *(1.52–4.15)*	0.159
Female	90 (56.25)	2.9 ± 1.37 *(1.46–3.67)*	
t* Independent t-test was used to compare the means SD – standard deviation			

Tab. 5. *Comparison of urinary bladder wall thickness among diabetic men and women*

Urinary bladder wall thickness in mm *n* (%)		Study participant Mean ± SD *(range)*	p value
Male	30 (37.5)	3.66 ± 1.61	**0.027**
Female	50 (62.5)	2.9 ± 1.37	
t* Independent t-test was used to compare the means SD – standard deviation			

Tab. 6. *Relationship of diabetes mellitus duration with urinary bladder wall thickness*

Urinary bladder wall thickness in mm *n* (%)		T2DM Mean ± SD *(range)*	P value
<6 year duration	43 (53.75)	1.16 ± 0.37	0.231
>6 year duration	37 (46.25)	1.22 ± 0.42	
* Independent t-test was used to compare the means SD – standard deviation			

Tab. 7. *Association between urinary bladder wall thickness, glycaemic control, urinary bladder volume and duration of diabetes mellitus in type 2 diabetes mellitus patients*

Variables	*N*	rho*	*P* value
BWT	78	0.119	0.309
HBA_{1c}	78		
BWT	80	–0.009	0.937
UBV	80		
BWT	80	–0.163	0.148
DDM	80		
* Spearman's rank correlation was used to check the relationship			
BWT – bladder wall thickness; HBA_{1c} – glycated haemoglobin; UBV – urinary bladder volume; DDM – duration of diabetes mellitus			

Tab. 8. *Predictors of urinary bladder wall thickness*

Variables	*N*	*Statistic*	*p* value
Age	80	0.44	0.665
Sex	80	–2.33	0.023
BMI	80	–0.62	0.537
DDM	80	–0.92	0.362
HBA_{1c}	80	0.90	0.369
FBG	80	1.04	0.300
* Multiple regression analysis was used to determine the predictor of UBW BMI – body mass index; UBW – urinary bladder wall thickness; DDM – duration of diabetes mellitus; HBA_{1c} – glycated haemoglobin; FBG – fasting blood glucose			

1.46–3.67 mm, respectively. The mean urinary bladder wall thickness of all male and female participants of the study were 2.84 ± 1.31 mm and 2.90 ± 1.37 mm, respectively. There was no statistically significant difference in the urinary bladder wall thickness ($p = 0.159$) between the males and females who participated in this study (Tab. 4) (Fig. 2). However, the ranges of the urinary bladder wall thickness in the diabetic male and female subjects were 3.66 ± 1.61 mm and 2.9 ± 1.37 mm, respectively. There was a statistically significant difference in the urinary bladder wall thickness between the diabetic men and women ($p = 0.027$) (Tab. 5).

The association between urinary bladder wall thickness and glycaemic control in type 2 diabetes mellitus patients

Using Spearman's rank correlation to test the relationship between the glycaemic control of diabetic subjects and the mean urinary bladder wall thickness, there was no correlation between these variables (Spearman's rho = 0.119, $p = 0.309$).

Relationship of diabetes mellitus duration with urinary bladder wall thickness

The mean duration of diabetes mellitus in the diabetic subjects was 7.15 ± 5.62 years with a range of 0.3–34 years, while the median was 6 years. The skewed distribution of the duration of DM led to the use of the median of 6 years in the grouping of DM patients to those with a duration of diabetes mellitus below 6 years and those above 6 years. Comparing the mean urinary bladder thickness of diabetic patients whose duration of diabetes mellitus was below 6 years with those above 6 years showed that there was no statistically significant difference between them ($p = 0.231$) as shown in Tab. 6. The urinary bladder thickness and duration of diabetes mellitus in diabetics were not normally distributed, hence Spearman's rank correlation was used to test the relationship between these continuous variables. This yielded a Spearman's rho of –0.163 ($p = 0.148$) in Tab. 7, meaning that there was no linear relationship between these variables. These findings show that the duration of diabetes mellitus does not determine the urinary bladder wall thickness.

Predictors of urinary bladder wall thickness

A multiple regression analysis was run to predict urinary bladder wall thickness from age, gender, BMI, duration of diabetes mellitus, fasting blood glucose and glycated haemoglobin level. Among all six variables, only gender added statistically significantly to the prediction, $p = 0.023$ (Tab. 8).

Discussion

The age range distribution in this study (40–85 years) was similar to a related study by Uzun *et al.*[31] who also carried out their study among patients aged 40 to 75 years.

Among the 80 diabetic mellitus patients included in this study, only three (3.75%), who were females, presented with urinary tract symptoms. This is similar to the findings in the study done by Salem *et al.*[32], where only two (10%) of the 20 non-neuropathy diabetic patients had obstructive and overactive symptoms. Also, 22 (36.7%) out of the 60 neuropathy diabetic patients presented with lower urinary tract symptoms. 20% of the diabetic neuropathy patients presented with obstructive urinary symptoms, while none of the non-neuropathy patients suffered from these symptoms. Urgency was the most common symptom in all the patients in the study done by Ali *et al.*[33]; urinary frequency which was the second common symptom, was recorded in 93.5% of the 62 patients with overactive bladder (OAB) and 63.9% (23) of the control group.

A common finding in the majority of reviewed studies was that the urinary bladder wall thickness was higher in the diabetics, patients with detrusor overactivity and urinary tract infection than in the non-diabetics. In the study carried out by Uzun *et al*[31], it was found out that women that were diabetic and had OAB syndrome had significantly increased bladder wall thickness compared with the controls (p = 0.000), which was similar to the findings in this study, whereby the mean urinary bladder wall thickness in the diabetic patients was 3.18 ± 1.50 mm greater than in the non-diabetic patients, which was 2.18 ± 0.41 mm, with a statistically significant difference between the two groups (p <0.001). In the study done by Ali *et al.*[33], bladder wall thickness (BWT) in the patients with documented detrusor overactivity was significantly higher than in the patients with normal cystometry. Bladder wall thickness values in patients diagnosed with cystitis cystica via cystoscopy and those with recurrent urinary tract infection (UTI) almost completely overlapped and were very similar. That of the patients with an episode of cured UTI (Group C) and the healthy controls (Group D) were almost the same in Milosevic *et al.*'s study[34]. The authors suggested that by measuring the BWT, one can differentiate between the patients with endoscopically verified cystitis cystica and healthy subjects.

The range of urinary bladder wall thickness in men (1.52–4.15 mm) was similar to that of women (1.46–3.57 mm) in this study population, and there was no statistically significant difference in the urinary bladder wall thickness (p = 0.159) between the males and females who participated in this study (Tab. 4). This is similar to the findings reported by Blatt *et al.*[35], where even though the males (2.1 ± 0.54 mm) had a slightly thicker bladder wall than the females (1.9 ± 0.45 mm), there was no statistically significant difference between the male and female patients with a p value of 0.064. Also, a study carried out by Kanyilmaz *et al.*[36] among 95 healthy volunteers in Turkey showed that there was no statistically significant difference (p = 0.16) in the BWT of the men and women. This is contrary to the findings of the study done by Oelke *et al.*[37] (Germany and the Netherlands) that reported higher BWT in males than in females in a healthy population.

The mean urinary bladder wall thickness of all the male and female participants of this study was 2.84 ± 1.31 mm and 2.90 ± 1.37 mm, respectively. However, the range of the urinary bladder wall thickness was higher in the diabetic males (3.66 ± 1.61 mm) than in the diabetic females (2.9 ± 1.37 mm). There was a statistically significant difference between the urinary bladder wall thickness of the diabetic men and women (p = 0.027) (Tab. 5).

This is contrary to the findings in the study done by Salem *et al.*[32] among diabetic children, whereby the average value of bladder wall thickness was almost the same in both neuropathic and non-neuropathic diabetic patients probably due to a lesser duration of DM in these type 1 diabetes mellitus patients compared to the type 2 DM in the index study. Also, the mean rise in estimated bladder weight in patients with neuropathy and those without was similar. This observation can be attributable to the difference in the age range of the study population, and the geographical and cultural differences.

There was no correlation between the urinary bladder wall thickness and the urinary bladder volume among the diabetic patients, and no statistical significance was found in this study. Similar findings were reported in the study done by Kanyilmaz *et al.*[36] in Turkey among 95 healthy volunteers, which revealed that the bladder wall thickness was negatively correlated with the urinary bladder volume (r = –0.50) and bladder surface area (r = –0.57). The results obtained in the study were, however, higher and statistically significant. Also, ultrasound estimated bladder weight had a statistically significant correlation with the bladder volume (r = 0.36), bladder surface area (r = 0.48), and the BWT (r = 0.25). This is contrary to the general knowledge that the BWT depends on the degree of bladder filling, which might have been due to the difference in sample size compared to other similar studies. Oelke[23] revealed that in normal women the detrusor wall thickness reduced rapidly between 50 and 250 ml of bladder filling, and reached the peak and maintained the value of thickness thereafter, with unremarkable differences between 250 ml and the maximum bladder capacity.

The relationship between the BWT of the diabetic subjects in this study and their mean glycated haemoglobin levels showed no correlation (Spearman's rho = 0.119) and no statistical significance (p = 0.309).

The relationship between the duration of diabetes mellitus (DDM) of the diabetic subjects in this study and their mean urinary bladder wall thickness showed no correlation (Spearman's rho = –0.163) and no statistical significance (p = 0.148). The reason could have been the fact that most of the diabetic patients in the index study were only diagnosed a few years ago, with the median duration of diabetes mellitus being six years, since it is of a non-parametric distribution. Longer duration of DM is associated with the development of thickened bladder wall. About half (53.75%) of the diabetic patients in this study had a DDM of less than six years, with a mean BWT of 1.16 ± 0.37 mm, while the other 46.25% with a DDM exceeding six years from being diagnosed with diabetes mellitus were found to have their mean BWT slightly

higher, measuring 1.22 ± 0.42 mm, but with no statistically significant difference ($p = 0.231$). All the patients in this study that presented with urinary symptoms had poor glycaemic control, with glycated haemoglobin levels in the range of 9–11%. Evidence suggested an increased prevalence of urgency with or without urge urinary incontinence among women with type 2 diabetes in the study done by Brown *et al.*[17] that involved 7,949 community dwelling women in the USA, and an increasing pattern with a longer duration of diabetes[18]. This was not the same in the study done by Salem *et al.*[32], where the duration of diabetes was found to be statistically significant in relationship with the ultrasound estimated BWT ($p = 0.018$), but not significantly related to any of the recorded urodynamic parameters in their study.

In the study by Ali *et al.*[33], using two-way ANOVA, it was revealed that there was a significant relationship between the BWT and DO ($p < 0.001$) and a non-significant relationship between the BWT and gender ($p = 0.142$). They also noted a positive correlation between the patients' age and BWT, which was non-significant both in detrusor overactive patients and healthy ones (*Pearson correlation*: $r = 0.266$, $p = 0.117$, and $r = 0.090$, $p = 0.486$, respectively). A multiple regression analysis done in the index study was run to predict urinary bladder wall thickness from gender, age, BMI, duration of diabetes mellitus, fasting blood glucose and glycated haemoglobin level. The model had a statistically significant predictive power, as shown in Tab. 8. Among the six variables, only gender was a significant predictor of the urinary bladder wall thickness, $p = 0.023$ (Tab. 8), while the other variables were not.

Conclusion

The BWT of the T2DM patients was statistically higher than that of the non-diabetic controls ($p < 0.001$). The mean urinary bladder wall thickness of the diabetic patients was significantly higher than that of the healthy controls.

Gender was the only variable that significantly predicted the BWT on multiple regression analysis.

Conflict of interest

There is no conflict of interest of any sort.

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