The Prevalence of Causative Uti Among Diabetic and Non-Diabetic Patients

Manar Abd Alsalam Kamal[1], Qanat Mahmood Atiyea[2]
[1, 2]College of science, University of Tikrit, Tikrit, Iraq
Email: manarabdsalam@gmail.com

Abstract
Urinary tract infections (UTIs) are common in both diabetes & non-diabetic people alike. Because the germ that cause illness differ in their susceptibility to antibiotic from region to region and, it is necessary to monitor trends and susceptibility patterns of the most common organisms to antimicrobials on a regular basis. The goal of the study is to establish the uropathogen spectrum and antibiotic sensitivity pattern in individuals with clinically diagnosed UTI, both diabetic and non-diabetic. This study began from the January 2020 till the mid of January 2022. A total of five hundred (500) Diabetic &non-diabetic patients' urine samples were obtained. These were collected from patients of both sexes and different ages hospitalized in salah-aldin Hospital. our study shows that increase frequency of urinary tract infection in diabetic subject 148/250(59.2%) in comparision to control 117/250(46.8%). The isolates were identified according to morphological, cultural and biochemical characteristics and confirm by Vitek-2 compact. There is no a significant difference in the causative agent between diabetic &non-diabetic patients, Most prevalence symptoms among diabetic and non-diabetic was fever, dysuria, abdominal pain, vomiting, pyuria and hematuria, most causative agent of UTI was E.coli (40.5%) diabetic (47%) nondiabetic followed by K.pneumonia (23.6%) diabetic (22.2%) nondiabetic, S.aureus (12%) diabetic (17.9%) nondiaetic, P.aeruginosa (15.5%) diabetic (7.6%) nondiabetic, P.mirabilis (4.7%) diabetic (5.1%) nondiabetic and E.faecalis (3.3%) only within diabetic patients .
Keywords: UTI; diabetic; healthy

1. Introduction

Infection of (UTI) is a bacterial infection brought induced by the presence and development of bacteria of (Haider et al., 2010). we can be defined the UTI is colonization and invasion of the urinary tract's structures by microorganisms, bladder emptying that isn't complete, fluid intake, kidney stone,also another factors increased the risk of UTI is sex, diabetes, and pregnancy (Al-Dulaymi, 2005).
The pathogen is able to cause infection because of its virulence factors, which are either responsible for antibiotic resistance, by producing the -lactamase enzyme, boosting its adhesion and colonization of the inside surface. When pathogenic germs infiltrate the body of the host, at the first the pathogen must be adhere to the cell's surfaces.
The virus was transmitted by mucus or other fluids produced by the body's regular defense mechanism. If the bacteria did not adhere, they were thrown out. Bacterial attachment to the tissue of the host By assisting the immune system, it was a critical first step in many types of infection.To enable colonization, germs must be able to withstand the body's defense mechanisms.It's possible that this is the first stage of bacterial invasion into the human body.cells from mammals (Juuti, 2004; Al-Dulaymi, 2005; Atabek, 2006).In people with diabetes mellitus, urinary tract infection (UTI) has long been recognized as a significant concern (DM) In a recent study,by de Aguiar and colleagues (1997).In diabetic admissionsUrinary tract infection was the most prevalent cause of infection (UTI) (Geerling etal.,1997). Bacterial adherence to the uroepithelium has changed (Gallacher etal.,1995). All of these factors are involved in the pathogenesis of UTI in diabetics, including granulocyte dysfuntion and antioxidant systems engaged in bacterial activity (Delamaire etal.,1997).

2. Material and Method

Collection of samples

UV sterilized polycarbonate vials with air-tight screw cap closures
were used to collect mid-stream urine samples of about 10-15 cc in the
early morning. A total of 500 samples were obtained from outpatients and
inpatients with diabetes and non-diabetes admitted to Salah Aldin
Hospital. Female patients were given a piece of cotton soaked in
potassium permanganate KMnO4 to disinfect their vagina before
urination, and the urine collection approach was clearly described to
them. A reference code, age, sex, and collection time were all written on
each urine sample bottle. The samples were transported to the laboratory
in a cool box, where they were maintained until the analyses were
completed (Vandepitte et al., 2003). All of the samples were sent to the
microbiological lab for testing.

doi.org/10.31838/hiv22.02.507 Received: 27.05.22, Revised: 10.07.22, Accepted: 16.08.22

Detection by Urine dipstick

To undertake a preliminary study of urine samples for UTI, dipstick
urine testing strips were utilized (URIPATH-U.K.). During first 2 hrs of
collecting the samples, this was completed. The strip has been
immersed in freshly voided urine at the temperature of the room for
approximately 2 sec. The color reaction has been specified through the
comparison of the immersed strip color to container's code. Leukocyte
esterase levels were evaluated following 2 mins and categorised as
negative, trace, small (+1), moderate (+2), or large (+3). The nitrite level
has been tested after 60sec and classified as positive or negative. With the
use of the same strip, the pH of urine samples was determined (Eyong et al., 2011; Darko, 2012; Pezzlo, 1988).

3. Culturing

The samples of the urine have been cultured on the blood and Mac
Conkey agar and incubated for a period of 24 hrs at a temperature of 37
Celsius following being gently mixed and inserting the calibrated loop
vertically (Collins etal., 2004(
The urine has been gathered into the sterile screw-capped testing tubes
and cultivated immediately on Blood and MacConkey agar (with the use
of calibrated loop).
Bacteria Isolation
After collection, clinical samples have been grown on the Blood and the
Mac Conkey agar and incubated for 24 hrs at a temperature of 37 o
Celsius. A single colony of bacteria growing on medium has been re-
cultured on the nutrient agar for obtaining the pure culture.

4. Result

Incidence of urinary tract infection

The incidence of UTI in tikrit City was 66.8% [334/500] in our study cohort. The diagnosis of UTI should be suspected in any diabetic patient and non-diabetic with symptoms consistent with UTI. These symptoms: frequency, urgency, dysuria, and suprapubic pain for lower UTI; and costovertebral angle pain/tenderness, fever, and chills, with or without lower urinary tract symptoms for upper UTI
,our study show that increase frequency of urinary tract infection in diabetic subject 148/250(59.2%) in comparision to control 117/250(46.8%),table(1).

Table (3) incidence of UTI in diabetic and non-diabetic patients

	diabetic	Non-diabetic	total
With UTI	148	117	265
Without UTI	102	133	235
total	250	250	500

Table (4) Demographic and clinical characteristics of participants in the diabetic group (n = 250) and non-diabetic group (n = 250)

Patient characteristic	Diabetic groupn=250	Non-diabetic group n=250
Gender		
Male	125(50%)	125(50%)
female	125(50%)	125(50%)
Age in year		
Less than 40	38(15.2%)	74(29.6%)
40-60	109(43.6%)	85(34%)
Above 60 years	103(41.2%)	91(36.4%)

Among 500 participate in the study (250 patients were diabetic &non-diabetic patients) the ddiabetic & non-diabetic patients who positive for urinary tract infection in diabetic group 74.7%(93 /125)patients were female and 44% (55/125) patients were male ,thirty two patients 25.6%(32/125)of Female diabetes patients who tested negative for urinary tract infection,while56% (70)patients were male , in non-diabetic group60%(75/125) patients were female and33.6% (42/125)patients were male ,fifty patients 40%(50/125) 66.4 percent (83/125) of non-diabetic patients who tested negative for urinary tract infection were female. As show in the table (5)

Table (5) Incidence of urinary tract infection in diabetic and non-diabetic group according to the gender

NO	Diabetic group n=250	Non-diabetic groupn=250
total	148(59.2%)	117(46.8)
female	93/125(74.7%)	75/125(60%)
male	55/125(44%)	42/125(33.6%)

There was an overall significantly higher incidence of uti in diabetic and non- diabetic women, than men (74.7%,60%) in comparision with male (44%,33.6%) ,

distribution of UTI by symptoms of UTI in both diabetic and non-diabetic patients

Atotal of 117 non- diabetic and 148 diabetic the most frequent symptom of a urinary tract infection is fever. presenting symptoms fever is seen among 65(43.9%) case in diabetic patients and 50(42.7%) case of non-diabetic patients,dysuria 35 (23.6%) of diabetic and 22(18.8%) of non- diabetic ,abdominal pain among 20(13.5%) diabetic and 23(19.6%) non –diabetic ,vomiting among 17(11.4%) of diabetic and 15 (12.8%) of non-diabetic ,hematuria among 4(2.7%) of diabetic and 2(1.7%) of non-diabetics,pyuria among 7(4.7%) of diabetics and 5(4.2%) of non-diabetics

symptoms	Diabetes n=148	Non-diabetesn=117
Fever	65(43.9%)	50(42.7%)
Dysuria	35(23.6%)	22(18.8%)
Abdominal pain	20(13.5%)	23(19.6%)
Vomiting	17(11.4%)	15(12.8%)
Pyuria	7(4.7%)	5(4.2%)
hematuria	4(2.7%)	2(1.7%)

distribution of UTI according to age

The average age of diabetic and non-diabetic patients
categorized in three group, (less than 40 years and 40-60 years and more than 60 years) among less than 40 years there are 38(15.2%) diabetic and74(34%) non-diabetic ,40-60 years there are 109(43.6%) diabetic and 83(34%) non-diabetic, above 60 years there are 103(41.2%) *etal.*,2013).diabetic and 91(36.4%)non-diabetic as show in the table (7)

Table (7) diatribution of prticipants by age		
Patients age	Diabetic group n=250	Non-diabetic group n=250
Less than 40 years old	33(13.2%)	40(16%)
40-60 years old	127(50.8%)	132(52.8%)
Above 60 years old	90(36%)	78(31.2%)

Table (8) distribution of UTI in diabetes and non-diabetes patients according to age				
diabetic	Less than 40 years	40-60 years	Above 60 years	total
Positive UTI	19/33(57.5%)	75/127(59%)	54/90(60%)	148/250(59.2%)
Negative UTI	14/33(42.4%)	52/127(40.9%)	36/90(40%)	102/250(40.8%)
Non-diabetic	Less than 40 years	40-60 years	Above 60 years	Total
Positive UTI	15/40(7.5%)	72/132(58.5%)	30/78(38.4%)	117/250(46.8%)
Negative UTI	25/40(62.5%)	60/132(45.4%)	48/78(61.5%)	133/250(53.2%)

Bacterial causing UTI in diabetic and non-diabetic patients

500 urine samples from patients with and without diabetes were collected; the isolated bacteria were then chosen directly from the specimens by culturing the specimen on general and selective media; following incubation for 24 hours at 37 degrees Celsius, the growth bacteria were diagnosed biochemically and confirmed by Vitek2-compact according to Colle *et al.*, (1996) and Baron *et al.*, (1996), as shown in table (9)

Table (9) biochemical tests of gram-positive bacteria		
Biochemical test	S.aureus	E.faeclis
Catalase	+	_
Coagulase	+	
Gram stain	+	+ diplococci (or) short
Motility	_	_
Oxidase	+	_
Colour on MSA	yellow	Pink
Growth on macConkey agar	_	+
Susceptibility to novobiocin	+	

Table (10) biochemical test of gram-negative bacteria				
Biochemical test	E. coli	klebsiella	P.mirabilis	P.aeruginosa
Catalase	+	+	+	+
Oxidase	_	_	_	+
Gram stain	red	red	red	Red
Citrate utilization	–	+	+	+
H2S production	_	_	+	_
Indol production	+	–	–	–
Methyl red	+	_	+	_
KIA	A/A	A/A	A/A	K/K
Urease production	–	+	+	–
VP	_	+	_	_
Colour on MaConckey	purple	Purple mucoids	pale	pale

The bacteria that cause UTI in diabetes individuals are quite similar to those that cause With a few instances, UTI in non-diabetic people. In our analysis, the majority of infections found were gram negative enteric microbes, which are prevalent causes of UTI. The most prevalent organisms among diabetes and non-diabetic patients were determined to be E. coli (40.5 %) and (47 %) in diabetic and non-diabetic patients, respectively. Among the diabetic patients investigated, the most often isolated organism was E.coli.,Klebsiella pneumonia (23.6%), Pseudomonas aeruginosa (15.5%), Staphylococcus aureus (12%) Other microbes that were isolated less often Proteus mirabilis and Enterococcus faecalis.in non diabetic patients the most prevalence was E.coli followed byK.pneumoniae
(22.2%),S.aureus(17.9%),P.aeruginosa (7.6%) and less frequently isolated P.mirabilis .

Table (11) bacterial distribution type between diabetes and non-diabetes		
Bacterial sp	Diabetic patients	Non-diabetic patients
Escherehia coli	60/148(40.5%)	55/117(47%)
Klebsiella pneumoniae	35/148(23.6%)	26/117(22.2%)
Staphylococcus aureus	18/148(12%)	21/148(17.9%)
Pseudomonas aeruginosa	23/148(15.5%)	9/117(7.6%)
Proteus mirabilis	7/148(4.7%)	6/117(5.1%)
Enterococcus faecalis	5/148(3.3%)	0%
Total	148/250(59.2%)	117/250(46.8%)

5. Discussion

isolation and identification of pathogenic bacteria and compare the dominant pathogenic type between two group our study shows that increased In comparison to non-diabetic people, diabetes people have a higher rate of urinary tract infection, according to our research. subject 148/250(59.2%) in comparision to control 117/250(46.8%), Our Finding higher were compared to research conducted in KNH, where the frequency was reported to be 11% and do not concur with the findings of the al-Sudan

research. where overall prevalence of uti 19.5% (hamdan etal.,2015). our study disagree presenting the findings of a research conducted in Nigerea were the prevalence of uti among diabetes patients was 36 % (maharjan etal.,2015) I believe that the increased incidence of urinary infection In our study, higher adherence to ureoepithelial cells was attributable to the rise of antibiotic-resistant bacteria that cause uti in diabetes patients, as well as reduced antibacterial activity due to sweet urine abnormalities in neutrophil function,further bacteria indeed growth better in urine with glucose(Akbar .,2001).

In diabetic patients, autonomic neuropathybladder dysfunction, inadequate bladder emptying, and urine stagnation, all of which promote microbial development (Yu et al., 2014). Immune system in diabetic patients there are many factors contribute to increased the risk of infection such as decrese of (T-cell mediated immunological response ,prostaglandin E,thrombozane B2,Leukotrine B4) & impaired of leukocyte adherence ,chemotaxis and phagocytosis ,Diverse types of bacteria occupy the urinary system of diabetes patients because of lowered immunity, glucoseuria, bladder malfunction, and a lack of local urinary cytokines, according to an Akert study (Akert etal.,2013).

the an overall significantly a greater rate In both diabetic and non-diabetic women, uti can occur.,than men (74.7%,60%) in comparision with male (44%,33.6%) , A variety of men-related characteristics, such as the length of the urethra, the distance between the urogenital meatus and the anus, and the antibacterial qualities of the prostatic fluid, I believe, can explain the large difference. , but these differences are greater in diabetic subjects than in non-diabetic subjects, and Escherichia coli expressing type one fimbriae adhere better to ureoepethelial cells of diabetic women. (Mnif etal.,2013). it is well recognized known that urinary tract infection are takes the second rank after respiratory tract infection as aproblems encountered by particing physicians,Various research have confirmed a greater frequency of UTI among females in the diabetes and non-diabetic groups, as well as in the general population.our study disagree with Gorter etal.,2012 demonstrate that more male than female participants tested positive for UTI (22.4 % in female vs. 17.8 % in male) and contradict the findings of a research conducted in Alsudan, which found that men had a greater UTI frequency than females (22.3 % vs. 15.1 %) (Hamdan etal.,2015) Which supports the findings of a research done in the United Arab Emirate (UAE), which indicated that diabetes females have a higher prevalence of UTI than diabetic males (37 percent versus 34 percent) (Mubarak etal.,2012). Another research in Saudi Arabia contradicted the conclusions of this one, indicating that there was a link between gender and UTI among diabetics (Al-Rubeaan etal.,2013). Canadian research found that diabetes women were 6-15 times more likely than non-diabetic women to be hospitalized for acute pyelonephritis. (Flores-Mireles etal.,2012).

When comparing UTI symptoms in diabetic and non-diabetic patients, we discovered that diabetes patients had more fever and dysuria, whereas other symptoms were similar in both groups. This is in contrast to Sahib.,2008, who discovered that diabetes patients had considerably greater fever, dysuria, and urination problems, pain in the abdomen vomiting, and hematuria than non-diabetic patients (Sahib.,2008) According to earlier research UTI is increased considerably raised when the age increased (Tektook etal.,2017). Other research, on the other hand, discovered no correlation between age and a higher prevalence of UTI in those with diabetes (Al-Rubeaan etal.,2013). Among our study, UTI risk was greater in those with diabetes who had been diagnosed for more than 40 years. I think this is because of how diabetes affects people over time. , such as a suppressed immune system and neuropathy (Akert etal.,2013). Previous research has found a similar rise in risk for diabetic people over the age of 40. (Abdulla etal.,2015). Long-term diabetes can cause cytopathy, neuropathy, and renal papillary necrosis, all of which can lead to UTI (Nawaz.,2008). Another research, on the other hand, discovered in diabetic individuals, the duration of diabetes had no effect on the risk of UTI (Al-Rubeaan etal.,2013).

UTI was seen in increasing order of age whearas in non-diabetic patients, the incidence of UTI was highest in the patients between 40-60 years age groups, In both ddiabetic and non-diabetic patients, our research found a substantial link between patient age and the occurrence of urinary tract infections. In his investigation, Mahrjan MN et al. made a similar observation. Several research revealed that the incidence of illness in the urinary tract in women are more likely than males (Akbar.,2001). However, Khadka et al.,2012 found that UTI occurs more commonly in people aged 31-40 years, followed by those aged 41-50 years. Patients with diabetes for more than 15 years have been discovered to have a comparable rise in risk in previous studies (Debora and Simão, 2007). I believe that long-term effects of diabetes, such as a suppressed immune system and neuropathy, as well as the possibility of cytopathy, nephropathy, and renal papillary necrosis—all of which increase the risk of UTI—are to blame for the elevated risk of UTI in patients with diabetes who have had it for more than 40 years (Manjunath etal.,2011).

This study showed that K.pneumoniae was the organism that was isolated the second most frequently. in both diabetes and non-diabetic individuals, which is consistent with Acharya D et al, (2015) and (Akbar., (2991)study where the dominating organism was E.coli,According to several studies, E.coli is the most prevalent uropathogen (Nitzan et al., 2015). I believe that E. coli is a Because this bacteria clings to uroepithelial cells by attaching to glycolipid present on their cell membrane through p fimbriae, it is a more prevalent cause of UTI in

diabetes and non-diabetic patients As a result, it has significant virulence factors, Although E.coli virulence factors have been studied the most, many of the same ideas might be applied to other uropathogens. Klebsiella (Hoepelman etal.,2015). This study is consistent with others, which show that gram-negative bacteria, particularly E. coli, remain the most prevalent pathogen recovered in UTI patients (Yismaw etal, 2012).

Reference

Abdulla MC, Jenner FP, Alunga J. Urinary tract infection in type 2 diabetic patients: risk factors and antimicrobial pattern. Int J Res Med Sci 2015;3(10):2576-9.

Acharya A, Gautam R, Subedee L: Uropathogens and their antimicrobial susceptibility pattern in Bharatpur, Nepal. Nepal Med Col J 2011, 13(1):30-33.

Akbar DH. Urinary tract infection: Diabetics and non-diabetic patients. Saudi Medical Journa.l 2001; 22(4):326-329.

Akter T, Mia Z, Shahriar M. Antibiotic Sensitivity of Pathogens Causing Urinary Tract Infection. Bangladesh Pharmaceutical Journal 2013;16(1): 53-8.

AL-Dulaymi, M. (2005). Study The Effect Of (632.8 nm) Helium-Neon on Some Virulence Factors of Staphylococcus aureus and Escherichia coli. M.Sc. Thesis, Univ. of Baghdad.

Al-Rubeaan K, Moharram O, Al-Naqeb D, Hassan A, Rubbean HA. Prevalence of urinary tract infection and risk factors among Saudi patients with diabetes. World J Urol. 2013;31(3):573–578.

Atabek, A. (2006). Investigating bacterial outer membrane polymers and bacterial interactions with organic molecules using atomic force microscopy. Worcester Polytechnic Institute.

Collee,G.J. Marmion, P. B. Fraser, G. A. Simmons, A. (1996). Mackie & McCartney Practical Medical Microbiology.14th edition. Churchill Livingstone Inc. USA.

Craig J, Simpson J, Williams G, Lowe A, Reynolds G, McTaggart S, et al. Antibiotic prophylaxis and recurrent urinary tract infection in children. N Engl J Med 2009; 361:1748-59.

Debora da Silva Krenke1, Simão Augusto Lottenberg. Comparison of agents and sensitivity profile in urinary tract infection in diabetic and non-diabetic patients. einstein. 2007; 5(4):363-367.

Delamaire M, Maugendre D, Moreno M, Le Goff MC,Allannic H, Genete B. Impaired leucocyte functions indiabetic patients. Diabet Med 1997; 14: 29-34.

Flores-Mireles AL, Pinkner JS, Caparon MG, Hultgren SJ. EbpA vaccine antibodies block binding of Enterococcus faecalis to fibrinogen to prevent catheter-associated bladder infection in mice. Sci Transl Med. 2014; 6:254ra127. This is the first study to dissect the mechanism of E. faecalis infection during a CAUTI; this work led to the development of a vaccine that prevents infection in a mouse model of a CAUTI.

Gallacher SJ, Thomson G, Fraser WD, Fisher BM, Gemmell CG, MacCuish AC. Neutrophil bactericidal function in diabetes mellitus: evidence for association with blood.

Geerling SE, Erkelens DW, Hoepelman IM. Urinary tract infection in patients with diabetes mellitus. Ned Tijdschr Geneeskd 1997; 141: 372-375.

Hamdan H,Kubbbara E,Adam A,Hassan O, S uliman S.Urinary tract infections and antimicrobial sensitivity among diabetic patients at Khartoum,Sudan.Annals of clinical microbiology and antimicrobials .2015;vol 14 ,Issue 26.

Hoepelman IM, Meiland R, Geerling SE. Pathogenesis and management of bacterial urinary tract infections in adult patients with diabetes mellitus. Int J Antmicrob Agents, 2003; 22: S35-S43.

Juuti, K. (2004). Surface protein Pls of methicillin-resistant Staphylococcus aureus _ role in adhesion, invasion and pathogenesis, and evolutionary aspects. Thesis. Univ. of Helsinki.

Khadka KS, Khadka J, Binod L, Shrestha R. Indices of UTI among the patients visiting western regional hospital pokhara, Nepal. JHAS 2012; 1:35-37.

Lloyds S, Zervas M, Mahayni R, Lundstrom T. Risk factors for enterococal urinary tract infection and colonization in a rehabilitation facility. Am J Infect Control1998; 26:35-9. London, New York.

Maharjan MN et al. Comparative Study among the Bacterial Causes of Urinary Tract Infection in Diabetic and Non-Diabetic Patients Visiting Alka Hospital, Lalitpur. Ann Clin Med Microbio. 2015;1(2):1006-1014.

Mnif, M., Kamoun, M., & Kacem, F. (2013). Complicated urinary tract infections

Mo F, Ma J, Yang X (2020) In vitro and in vivo effects of the combination of myricetinand miconazole nitrate incorporated to thermosensitive hydrogels, on C. albicans biofilms. Phytomedicine.

Mubarak, A. A., Ashraf, A. M., El-hag, M., Raza, M. A., Majed, A., Al-Sharbatti, S.

Muhammad M. H. Swedan S. Molecular and phenotypic characterization of carbapenems resistance and extended spectrum beta-lactamases among urinary Escherichia coli isolates. Int J Sci Tech 2015; 5:1-14.

Nawaz M. Isolation and characterization of tetracycline resistant Citrobacter spp. from catfish. Food Microbiol 2008;25: 85-91.

Nitzan, O., Elias, M., Chazan, B., & Saliba, W. (2015). Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management. Diabetes Metab Syndr Obes. 2015; 8: 129–136.

Tektook NK, Al- Lehibi KI, Al-Husseinei RK. Prevalence Some Pathogenic Bacteria Causing UTI in Diabetic Patients in Specialized Center for Endocrinology and Diabetes of Baghdad City–Iraq. Medical Journal of Babylon 2017; 14(2):260 –6.

Yismaw G, Asrat D, Woldeamanuel Y, Unakal CG.Urinary Tract Infection: Bacterial etiologies, drugresistance profile and associated risk factors in diabetic patients attending Gondar University Hospital, Gondar,Ethiopia. Euro J Exp Bio 2012; 2(4):889-98.

Yu S, Fu AZ, Qiu Y, Engel SS, Shankar R, G. Brodovicz K, et al Disease burden of urinary tract infections among type 2 diabetes mellitus patients in the U.S. J Diabetes Complications 2014;28:621-26.