Prevalence of diabetic kidney disease in patients with type 2 diabetes mellitus
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Introduction
Diabetes mellitus (DM) is one of the leading causes of chronic kidney disease (CKD) which is associated with increased morbidity and mortality worldwide [1]. Diabetic nephropathy (DN) has also become the main leading cause of end-stage renal disease (ESRD) and cardiovascular mortality. In such patients this condition appears after many years of diabetes onset [2]. Despite all pharmacologic therapies available for DN treatment, many patients develop kidney damage. DN affects about one-third of the patients with type1 DM and 25% of patients with type 2 DM [3]. Various postulated mechanisms for DN are hyperglycemia (causing hyperfiltration and renal injury), advanced glycation end products, and activation of cytokines [4].

The overall prevalence of microalbuminuria (MA) and macroalbuminuria in both types of diabetes is ~30–35%. Both MA and macroalbuminuria increase mortality from any cause in DM [5]. MA independently predicts cardiovascular morbidity and was found to be associated with increased risk of coronary and peripheral vascular disease and death from cardiovascular disease in the general nondiabetic population [5].

Patients and methods
Study design and population
This observational study was approved by the local Institutional Ethics Committee and conformed to the Helsinki Declaration and carried out on type 2 diabetic patients who were attending the specialized diabetes and nephrology clinics of Internal Medicine.
Department, Zagazig University Hospitals from January 2018 to June 2018. It included a total number of 151 patients with type 2 DM, 88 are men and 63 are women. Informed written consents were obtained from the patients. Inclusion criteria: type 2 DM of more than 10 years and age more than 40 years old at onset of DM. Exclusion criteria: dependence on insulin therapy or type 1 DM, current urinary tract infection, history of CKD before the onset of diabetes, known malignancy, known hereditary disease, systemic disease (other than DM) known to cause CKD, patients under medications affecting kidney function and urinary protein excretion, recent attack of acute kidney injury during the last 6 months and obesity.

Physical examination and measurements
All patients were submitted to full history taking, clinical examination, and these investigations including: complete blood count, fasting blood glucose and glycosylated hemoglobin (HbA1c), blood urea, serum creatinine, serum uric acid, calculation of estimated glomerular filtration rate (eGFR) using modification of diet in renal disease equation: 
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eGFR (\text{ml/min/1.73 m}^2) = 175 \times (\text{serum Creatinine})^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female})
\]
[6], lipid profile, serum albumin, urine analysis, urinary albumin to creatinine ratio, and pelvic abdominal ultrasound.

Statistical analysis
All data were collected, tabulated and statistically analyzed using SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA) & MedCalc 13 for windows (MedCalc Software bvba, Ostend, Belgium). Qualitative data were represented as frequencies and relative percentages. \(\chi^2\) test was used to calculate the difference between qualitative variables. Quantitative data were expressed as mean±SD. Analysis of variance \(F\) test was used to calculate the difference between quantitative variables in more than two groups in normally distributed data. The significance level for all the above-mentioned statistical tests was done. The threshold of significance is fixed at 5% level (Pvalue). A \(P\) value of more than 0.05 indicates nonsignificant results; \(P\) value of less than 0.05 indicates significant results; and \(P\) value of less than 0.01 indicates highly significant results.

Results
Our results show that 28.5% of the studied patients have abnormal ultrasound findings, 45.7% have diabetic retinopathy, 30.5% have abnormal urine analysis, and 28.5% of the studied patients had hypertension. It was also shown that 60.3% of the patients have normoalbuminuria, 31.8% have MA, and 7.9% have macroalbuminuria. Regarding GFR stages, 25.8% of the patients are of G1, 31.8% G2, 16.6% G3a, 16.6% G3b, 6.6% G4, and 2.6% are of G5 (Table 1). There is a statistically significant increase in grading in patients having macroalbuminuria; also most normoalbuminuric patients are of G1 and G2 (Table 2). In our study, 53.6% of the studied patients are at low risk of CKD, 9.9% are at moderate risk, and 36.4% are at high risk (Table 3) and the degree of risk on the studied patients was classified according to KDIGO 2012 [7] (Fig. 1). There is a statistically significant increase in the prevalence of hypertension, abnormal ultrasound, fundus and urine findings among high-risk cases compared with low and moderate cases and there is a statistically significant increase in systolic blood pressure, diastolic blood pressure, and mean arterial blood pressure among moderate and high-risk cases compared with low risk cases (Table 4). There is a statistically significant increase in the levels of fasting blood glucose, HbA1c, serum triglycerides, blood urea, serum creatinine, urinary albumin to creatinine ratio, and GFR among high-risk cases compared with moderate and high cases; also there is a statistically significant decrease in the levels of serum albumin among high-risk cases (Table 5).

| Variables | n (%) (N=151) |
|-----------|---------------|
| US        |               |
| Normal    | 108 (71.5)    |
| Changes in kidney size | 43 (28.5)    |
| Fundus    |               |
| Normal    | 82 (54.3)     |
| Established diabetic retinopathy | 69 (45.7)   |
| Urine analysis |       |
| Normal    | 105 (69.5)    |
| Abnormal  | 46 (30.5)     |
| HTN       |               |
| No        | 108 (71.5)    |
| Yes       | 43 (28.5)     |
| Albuminuria category |         |
| Normoalbuminuria (UACR < 30 mg/g) | 9 (60.3)    |
| Microalbuminuria (UACR 30–299 mg/g) | 48 (31.8)   |
| Macroalbuminuria (UACR ≥300 mg/g) | 12 (7.9)    |
| GFR grade |               |
| G1 (GFR≥90 ml/min) | 39 (25.8)   |
| G2 (GFR 60–89 ml/min) | 48 (31.8)   |
| G3a (GFR 59–45 ml/min) | 25 (16.6)   |
| G3b (GFR 30–44 ml/min) | 26 (16.6)   |
| G4 (GFR 15–29 ml/min) | 10 (6.6)    |
| G5 (GFR <15 ml/min) | 4 (2.6)      |

GFR, glomerular filtration rate; HTN, hypertension; UACR, urinary albumin to creatinine ratio; US, ultrasound.
Table 2 Comparison of albuminuria and glomerular filtration rate grading among the studied patients

| Albuminuria category | GFR grade | Normoalbuminuria (N=91) [n (%)] | Microalbuminuria (N=48) [n (%)] | Macroalbuminuria (N=12) [n (%)] | $\chi^2$ | P   |
|----------------------|-----------|-------------------------------|-------------------------------|-------------------------------|---------|-----|
| G1 (GFR ≥90 ml/min)  | 36 (39.6) | 3 (6.2)                       | 0 (0)                         |                               |         |     |
| G2 (GFR 60–89 ml/min)| 45 (49.5) | 3 (6.2)                       | 0 (0)                         |                               | 176.7   | <0.001|
| G3a (GFR 59–45 ml/min)| 9 (9.9)   | 16 (33.3)                     | 0 (0)                         |                               |         |     |
| G3b (GFR 30–44 ml/min)| 1 (1.1)   | 22 (45.8)                     | 2 (16.7)                      |                               |         |     |
| G4 (GFR 15–29 ml/min)| 0 (0)     | 4 (8.3)                       | 6 (50)                        |                               |         |     |
| G5 (GFR <15 ml/min)  | 0 (0)     | 0 (0)                         | 4 (33.3)                      |                               |         |     |

GFR, glomerular filtration rate. P value less than 0.05 is significant.

Table 3 Risk of chronic kidney disease progression among the studied patients

| Variables (risk) | Classification according to results | n (%) (N=151) |
|------------------|-------------------------------------|---------------|
| Low risk         | G1A1, G2A1                          | 81 (53.6)     |
| Moderate risk    | G1A2, G2A2, G3aA1                    | 15 (9.9)      |
| High risk        | G3bA1, A2 and A3, G4A2 and A3, G5A3 | 55 (36.4)     |

Figure 1

Progression of CKD by GFR and albuminuria categories. CKD, chronic kidney disease; GFR, glomerular filtration rate.
Type 2 DM is a public health concern worldwide and an important cause of morbidity and mortality. Type 2 DM is associated with microvascular and macrovascular complications. DN, which is characterized by proteinuria, is one of the most serious long-term microvascular complications of DM. The proportion of DN is increasing worldwide. DN is the leading cause of CKDs and ESRD [8].

Type 2 DM is a progressive disease whose prevalence also increases with age, thus exposing the patients to an increased risk of long-term diabetic complications, including diabetic kidney disease [9]. Without any intervention in type 2 diabetic patients, 20–40% with MA progress to manifested nephropathy after 20 years from the onset of diabetes; ~20% develop ESRD [10].

It is also known that DN is mostly characterized by increased urinary albumin excretion and loss of renal function. Increased urinary albumin (proteinuria) is a key component of this disease [11]. A systematic determination of urinary albumin to creatinine ratio and eGFR may contribute to an early diagnosis, thus allowing intervention during the initial stages of the disease when treatment is more efficient [11].

### Table 4 Comparison between risk of chronic kidney disease and different findings among the studied patients

| Variables (risk) | Low (N=81) [n (%)] | Moderate (N=15) [n (%)] | High (N=55) [n (%)] | $\chi^2$ | P |
|------------------|---------------------|-------------------------|---------------------|---------|---|
| Sex              |                     |                         |                     |         |   |
| Male             | 49 (60.5)           | 6 (40)                  | 33 (60)             | 2.29    | 0.32 |
| Female           | 32 (39.5)           | 9 (60)                  | 22 (40)             |         |     |
| HTN              |                     |                         |                     |         |   |
| No               | 68 (84)             | 11 (73.3)               | 29 (52.7)           | 15.71   | <0.001 |
| Yes              | 13 (16)             | 4 (26.7)                | 26 (47.3)           |         |     |
| US               |                     |                         |                     |         |   |
| Normal           | 67 (82.7)           | 11 (73.3)               | 30 (54.5)           | 12.79   | 0.002 |
| Change in kidney size | 14 (17.3) | 4 (26.7)                | 25 (45.5)           |         |     |
| Fundus           |                     |                         |                     |         |   |
| Normal           | 53 (65.4)           | 7 (46.7)                | 22 (40)             | 8.9     | 0.01 |
| Established diabetic retinopathy | 28 (34.6) | 8 (53.3)                | 33 (60)             |         |     |
| Urine analysis   |                     |                         |                     |         |   |
| Normal           | 66 (81.5)           | 12 (80)                 | 27 (49.1)           | 17.09   | <0.001 |
| Abnormal         | 15 (18.5)           | 3 (20)                  | 28 (50.9)           |         |     |
| Age (years) (mean±SD) | 55.07±5.72       | 52.53±5.89               | 54.29±6.97          | 1.12    | 0.33 |
| BMI (kg/m²) (mean±SD) | 25.47±1.95          | 25.98±2.58              | 26.04±2.73          | 1.08    | 0.34 |
| SBP (mmHg) (mean±SD) | 130.56±11.59        | 136.67±10.29            | 136.36±11.76        | 4.87    | 0.009 |
| DBP (mmHg) (mean±SD) | 79.75±8.66          | 83.33±9.94              | 84.91±10.39         | 5.05    | 0.008 |
| MABP (mmHg) (mean±SD) | 96.7±8.4            | 101.77±11.03            | 102.04±9.93         | 6.14    | 0.003 |

DBP, diastolic blood pressure; HTN, hypertension; MABP, mean arterial blood pressure; SBP; systolic blood pressure; US, ultrasound. P value less than 0.05 is significant.

### Table 5 Comparison between risk of chronic kidney disease and some laboratory investigations among the studied patients

| Variables (risk) | Low (N=81) [mean±SD] | Moderate (n=15) [mean±SD] | High (n=55) [mean±SD] | F | P |
|------------------|----------------------|---------------------------|-----------------------|---|---|
| Hb (g/dl) (mean±SD) | 11.93±1.24           | 11.65±0.97                | 11.81±1.37            | 0.35 | 0.7|
| FBG (mg/dl) (mean±SD) | 152.6±53.71          | 156.95±62.19              | 171.2±87.11           | 3.67 | 0.04|
| HbA1c (%) (mean±SD) | 6.56±0.97            | 6.86±1.08                 | 7.17±0.96             | 6.3  | 0.002|
| Cholesterol (mg dl) (mean±SD) | 193.02±42.42       | 204.4±55.53               | 196.9±48.68           | 0.42 | 0.66|
| TG (mg/dl) (mean±SD) | 156.52±58.62         | 175.2±44.18               | 189.14±64.3           | 3.27 | 0.04|
| Albumin (mg/dl) (mean±SD) | 4.36±0.5             | 4.17±0.46                 | 4.11±0.38             | 5.11 | 0.007|
| Urea (mg/dl) (mean±SD) | 46.84±32.14          | 44.8±16.24                | 55.68±29.77           | 3.65 | 0.04|
| S.Cr (mg/dl) (mean±SD) | 1.39±0.82            | 1.37±0.53                 | 1.71±0.9              | 3.71 | 0.04|
| Unig (mg/dl) (mean±SD) | 6.32±1.45            | 6.45±1.16                 | 6.59±1.71             | 0.51 | 0.6|
| UACR (mg/g) (mean±SD) | 74.36±150.72         | 36.28±39.06               | 104.68±149.95         | 4.56 | 0.01|
| GFR (ml/min) (mean±SD) | 70.67±25.52          | 57.53±21.06               | 57.89±27.38           | 4.65 | 0.01|

FBG, fasting blood glucose; GFR, glomerular filtration rate; Hb, hemoglobin; HbA1c, glycosylated hemoglobin; S.cr, serum creatinine; TG, triglycerides; UACR, urinary albumin to creatinine ratio. P value less than 0.05 is significant.

### Discussion

Type 2 DM is a public health concern worldwide and an important cause of morbidity and mortality. Type 2 DM is associated with microvascular and macrovascular complications. DN, which is characterized by proteinuria, is one of the most serious long-term microvascular complications of DM. The proportion of DN is increasing worldwide. DN is the leading cause of CKDs and ESRD [8].

Type 2 DM is a progressive disease whose prevalence also increases with age, thus exposing the patients to an increased risk of long-term diabetic complications, including diabetic kidney disease [9]. Without any intervention in type 2 diabetic patients, 20–40% with MA progress to manifested nephropathy after 20 years from the onset of diabetes; ~20% develop ESRD [10].

It is also known that DN is mostly characterized by increased urinary albumin excretion and loss of renal function. Increased urinary albumin (proteinuria) is a key component of this disease [11]. A systematic determination of urinary albumin to creatinine ratio and eGFR may contribute to an early diagnosis, thus allowing intervention during the initial stages of the disease when treatment is more efficient [11].
So, the aim of this study was to estimate the prevalence of diabetic kidney disease in patients with type 2 DM attending our outpatient clinics for regular follow-up visits; therefore early identification of DN would allow immediate intervention, thus diminishing the progression of renal disease and cardiovascular risk.

Our results show that 31.8% of patients had MA and 7.9% had macroalbuminuria. These findings are in agreement with that of another study which reported that in type 2 diabetic patients, the overall prevalence of MA and macroalbuminuria was 34.2 and 12.8%, respectively [12].

In Bahrain, the prevalence of MA and macroalbuminuria among type 2 diabetic patients were 22 and 5.8%, respectively [13]. Overall, between June 2006 and May 2007 in Kuwait, a result taken from patients with type 2 DM showed that the prevalence of MA was 58.2% [14]. In another setting of Kuwait, the prevalence rate of proteinuria among type 2 diabetic patients was found to be 43.5%, the prevalence of MA and macroalbuminuria was 27.3 and 16.2%, respectively [15]. In Sudan, the prevalence of MA among type 2 diabetic patients was 44% [16].

In Tunisia, the prevalence of MA among type 2 diabetic patients who were followed up in two primary health care centers was 23% [17]. Moreover, studies conducted in Asian countries reported variability in the prevalence rate of proteinuria ranging from 14.2% in Iran, 24.2% in Pakistan, to 36.3% in India, while the prevalence of macroalbuminuria was 12.7% in Taiwan and 11.2% in Thailand [18–20]. The prevalence of MA in European countries was 26.9% in Hungary, while macroalbuminuria was 16% in Italy as well as Sweden and 9% in Germany [21–24].

These variations in the prevalence rate of proteinuria can be attributed to the differences in several factors such as the study design, source of study population, sample selection, race, age, sex structure of the study population, diagnostic criteria, as well as the methods of measurement of proteinuria and urine collection, diabetic duration, diabetic treatment, and presence of hypertension.

According to GFR staging, our results have shown that 53.6% of the studied patients were in low risk, 9.9% were in moderate risk, and 36.4% were in high risk. This finding is similar to that reported by another study which reported that the prevalence for any type of CKD was 27.9% among their diabetic patients when 1145 patients were studied with type 2 DM in primary-care consults [25].

Analysis of our data has shown that there was a statistically significant increase in the levels of fasting blood glucose, HbA1c among high-risk cases compared with moderate and low cases. This finding supports the pathogenic role of hyperglycemia in inducing DN.

In our study, we found that 43 (28.5%) patients were hypertensive. The etiology of hypertension in DN involves mechanisms with multiple interrelated mediators that result in renal sodium reabsorption and peripheral vasoconstriction. In this respect, the results of our study disagree with that reported by another study which showed that the prevalence of hypertension in patients with type 2 DM was 13.37% [26]. The difference between the results may be due to the different sample size and population.

It is known that patients with overt DN (dipstick-positive proteinuria and decreasing GFR) generally develop systemic hypertension. Hypertension is an adverse factor in all progressive renal diseases and seems especially so in DN. Hypertension along with increases in intraglomerular capillary pressure and the metabolic abnormalities (e.g. dyslipidemia, hyperglycemia) likely interact to accelerate renal injury. The deleterious effects of hypertension are likely directed at the vasculature and microvasculature [26]. An evidence suggested that hypertension associated with obesity, metabolic syndrome, and diabetes may play an important role in the pathogenesis of DN. Central obesity, metabolic syndrome, and diabetes lead to increased blood pressure [27].

In our study, we found that 45.7% of the patients had established diabetic retinopathy which agrees with The Eye Diseases Prevalence Research Group which estimated that the prevalence rates for retinopathy and vision-threatening retinopathy in diabetic patients older than 40 years were 40.3 and 8.2%, respectively, and these were due to the microvascular complication of DM [28].

**Conclusion**

We detected proteinuria in 39.7% of the patients (31.8% of them had MA and 7.9% of them had macroalbuminuria); 25.8% of the studied patients were of G1, 31.8% G2, 16.6% G3a, 16.6% G3b, 6.6% G4, and 2.6% were of G5 and 28.5% of the studied patients had hypertension.
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Conflicts of interest
There are no conflicts of interest.

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