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Original Article

Assessment of kidney function and associated risk factors among type 2 diabetic patients

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ABSTRACT

Aim: diabetic patients are required for continuous monitoring programs hence continuous assessment of kidney function parameters is crucial. So, we aimed to determine the prevalence of Chronic Kidney Disease (CKD) and abnormal renal parameters, with poorly controlled type 2 diabetes mellitus pateints
Materials and methods: A cross-sectional study was carried out at private health care centre. A total of 300 diabetic patients aged 18 years and above attended the clinic from February 2018 to Dec 2018 were included. Socio-demographic, clinical, and laboratory data were obtained from the medical records of patients. Statistical analysis was carried out using (SPSS, version 23).
Results: out of the 300 diabetes patients recruited 42% of patients with type 2 diabetes had abnormal Creatinine Serum levels and 22.3% had abnormal glomerular filtration rate (GFR). Abnormal albumin urine levels were found in 28.3% and 11.3% had abnormal creatinine in urine. Abnormal Albumin: Creatinine Ratios (Alb/Cr), were found in 23%. Of the total, 77% (n = 231) had normal Alb: Cr Ratio, 20% had risk of nephropathy and 9% had nephropathy.
Conclusion: Current study revealed a high prevalence of abnormal renal parameters in patients with type 2 diabetes Mellitus. This necessitates the need for early and universal screening of renal functions. There is also an urgent demand for measures that target tight glycaemic, Vitamin D level and life style modifications is also required to all diabetic patients to achieve target value of HbA1C $\leq$ 7.

1. Introduction

On a global scale diabetes mellitus (DM) as a syndrome have been expanding, there isn't a single reason responsible for this inflation yet, around the world diabetic patients are now more aware and educated about their condition as they are a part of this growth [1]. But as the number of diabetic patients increases the fraction of patients with type 2 takes most of the ratio, as this type is occurring more commonly [2]. Due to the increase in its dominance each year this syndrome is considered as a heavy load on the medical field, while predicting the same pattern in developing countries [3]. With DM some patients develop complication in early stages and the recovery become much harder, but complication will happen eventually still we aim to delay these events as much as possible, while controlling patients' condition along any circumstances.

In respect to kidney complications, diabetes alone has a less effect on health as if present with kidney disease, more than one factor acts on the pathophysiology of developing kidney disease with diabetic patients, when patients are diagnosed at the start of diabetic kidney disease (DKD) the development will progress through stages, from reversible glomerular hyperplasia to renal dysfunction. DKD unfortunately is not always early identified but with continuous monitoring of a diabetic patient's sings of albuminuria (ratio of albumin to creatinine in urine above 30 mg/g) are considered as a start of this condition [4–6]. Basically, the markers observed when assessing the kidneys are the glomerular filtration rate (GFR), ratio of urine albumin/creatinine (Alb/Cr), and serum creatinine, the abnormal ratio of Alb/Cr alone is less threatening than appearing with abnormal GFR [7]. Genuinely the health status is different from one patient to another, due to the difference in age, gender, co-morbidities, genetics and many others. As in chronic kidney disease (CKD) multiple factors are affecting patient's condition, initiation, progression and improvement, for example in clinical practice both genders are treated and diagnosed equally but the hormonal difference in some cases could be significant, with male gender the prevalence of CKD was higher than females, and in

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addition to the resultant reduced GFR [8]. In contrast, a higher prevalence of kidney disease noticed in females rather than male patients, as poor glycaemic control had enhanced their condition [9]. In accordance to health condition vitamin D level appears to be an important factor effecting kidney disease, the significant number of CKD patients with vitamin D deficiency was related to this criterion, in addition to the complex relation of low vitamin D and increased albumin in urine [10,11]. The sum of diabetic patients' especially elderly, suffering from kidney disease is quite significant [12]. Still a similar prevalence was noticed in different countries around the world [13–15]. These finding mirror the importance of this condition on patient's quality of life, indeed the proper management and assessment of DKD can delay the progression of end stage renal disease [16].

2. Subject, material and methods

A Retrospective Observational Research design was chosen for data collection, the study was conducted in a health care centre in Ramallah district, Palestine. It comprised a sample of 300 diabetic patients randomly selected from a total of 500 patients, the duration of the study was from February 2018 to Dec 2018. The study was approved by the health and ethics committee of the health centre, and all the participants gave their informed consent in accordance with the Declaration of Helsinki [17]. Patient's data was reviewed from their visit's dates from 1st of January 2018 till 30th of December 2018. While the information collected included: demographic data, clinical laboratory tests and medication history only.

Laboratory tests include total glycated haemoglobin (HbA1c), Creatinine, glomerular filtration rate (GFR), Creatinine Urine, Albumin/Creatinine ratio, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Total Cholesterol, Triglyceride, High Density Lipoprotein, Low Density Lipoprotein, Vitamin D, Vitamin B12, Calcium, Albumin urine, Potassium, and Sodium.

Medication history include past and current medication in addition to past and present co-morbidities, but social variable was excluded due to unavailability of data such as marriage status, working hours and smoking status.

Inclusion criteria: Male and female patients diagnosed with type 2 diabetes mellitus, having a regular monitoring check-up including clinical laboratory tests, patients having laboratory tests assessing kidney function such as glomerular filtration rate and albumin/creatinine ratio, in addition to vitamin D test, patients with different co-morbidities with diabetes mellitus such as hypertension, dyslipidaemia and patients in use of medications.

Exclusion criteria: Male and female patients with type 1 diabetes, patients with gestational diabetes or pregnant females, non-diabetic patients and patients not having recent data specifically laboratory kidney function data.

3. Statistical analysis

The data was analysed using the Statistical Package for the Social Sciences (SPSS) version 23. Qualitative variables were summarized using frequencies and percentages. Graphical representations were provided for all relevant variables. The Chi-square and Fischer Exact tests were used to compare differences in proportions of qualitative variables. A simple and multiple binary logistic regression were used to investigate the association between the abnormal renal parameters and other significant risk factors. The stepwise method was used for variable selection and model building. A p value < 0.05 was chosen as the criteria to make decisions regarding statistical significance.

4. Results

4.1. Sociodemographic, anthropometric and biochemical characteristics of the participants

The demographic, anthropometric and biochemical characteristics of patients' is shown in Table 1. A total number of 300 patients with T2DM were included in this study. Among these patients 54% (n = 162) were male and 46% (n = 138) were female. The mean age ±S.D of the patients was 57 ± 8.5. The mean ± S.D of height, weight, BMI, HbA1c, FBS, Creatinine Serum, GFR, Albumin Urine, Creatinine Urine, Alb: Cr Ratio, and Vitamin D were 162.4 ± 9.5, 80.6 ± 13, 30.6 ± 24.6, 7.3 ± 1.3, 147 ± 41.2, 1.25 ± 1.2, 96.4 ± 25.4, 44.20 ± 117.7, 133.4 ± 77, 41.8 ± 151.6, 30.1 ± 10 respectively.

4.2. Prevalence of chronic kidney disease in patients with type 2 diabetes mellitus

Prevalence of different types of abnormal renal parameters in all the patients and in males and females are shown in Table 2. Overall, 42% (95% CI: 36.4%–47.6%) of patients with type 2 diabetes had abnormal Creatinine Serum levels (Creatinine Serum ˂0.72 mg/dL & ˃ 1.81) and 22.3% (95% CI: 17.6%–27.1%) had abnormal glomerular filtration rate (GFR ˂ 90 ml/min). Abnormal albumin urine levels (Albumin ˃ 23 mg/L) were found in 28.3% (95% CI: 23.2%–33.5%) and 11.3% (95% CI: 7.7%–15%) had abnormal Creatinine Urine (Creatinine˂ 37& ˃ 250). Abnormal Alb: Cr Ratios were found in 23% (95% CI: 18.2%–27.8%). Of the total, 77% (n = 231) had normal Alb: Cr Ratio, 20%(n = 60) had risk of nephropathy and 9% (n = 3) had

Table 1
Basic characteristics, anthropometric and renal profile parameters results for patients with T2DM.

Parameters	All patients (n = 300)			
	Mean	SD	Median	Inter quartile Range (Q1-Q3)
Age(years)	**57**	**8.5**	**57**	**52–62**
Height (cm)	**162.4**	**9.5**	**163**	**155–170**
Weight (kg)	**80.6**	**13**	**80**	**72–88**
BMI (kg/m2)	**30.6**	**24.6**	**30**	**27.6–33.3**
HbA1c (%)	**7.3**	**1.3**	**7**	**6.4–7.8**
FBS (mg/dl)	**147**	**41.2**	**140.5**	**119–164.5**
Creatinine Serum mg/dL	**1.25**	**1.2**	**0.85**	**0.68–1**
GFR ml/min	**96.4**	**25.4**	**94**	**80–112**
Albumin Urine mg/L	**44.20**	**117.7**	**10.2**	**4.75–30.75**
Creatinine Urine mg/dL	**133.4**	**77**	**122**	**77–180.6**
Alb: Cr Ratio mg/g	**41.8**	**151.6**	**8**	**4–22.5**
Vitamin D	**30.1**	**10**	**29**	**24–34.3**

Abbreviations: HbA1c, hemoglobin A1c; FBS, fasting blood sugar; GFR, glomerular filtration rate; Alb: Cr, albumin creatinine ratio; BMI, Body mass index.

Table 2
Prevalence of Abnormal renal parameters in male and female patients with type 2 diabetes mellitus.

Abnormal renal parameters	All (n = 300)	Female (n = 138)	Male (n = 162)	P. value
Creatinine Serum mg/dL				
0.72–1.81	174 (58%)	42 (30.4%)	132 (81.5%)	˂0.001
<0.72 & 1.81>	126 (42%)	96 (69.6%)	30 (18.5%)	
GFR ml/min				
≥90	233 (77.7%)	113 (81.9%)	120 (74.1%)	0.105
<90	67 (25.9%)	25 (18.1%)	42 (25.9%)	
Albumin Urine mg/L				
≤23	215 (71.7%)	104 (75.4%)	111 (68.5%)	0.190
>23	85 (28.3%)	34 (24.6%)	51 (31.5%)	
Creatinine Urine mg/dL				
37–250	266 (88.7%)	127 (92%)	139 (85.8%)	0.090
<37& > 250	34 (11.3%)	11 (8%)	23 (14.2%)	
Alb: Cr Ratio mg/g				
Alb: Cr < 30	231 (77%)	109 (79%)	122 (75.3%)	0.451
Alb: Cr ≥ 30	69 (23%)	29 (21%)	40 (24.7%)	

Abbreviations: GFR, glomerular filtration rate; Alb: Cr, albumin creatinine ratio index, p value < 0.05.

nephropathy. Of the 300 patients, 128 (42.78%) had only one abnormal renal parameter, 50 (16.7%) had two abnormal renal parameters and 49 (16.3%) had more than two abnormal renal parameters.

According to Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines; chronic kidney disease (CKD) defined as the GFR <60 ml/min or albumin creatinine ratio [ACR] ≥30 mg/g. Based on this, 69 (23%) chronic had chronic kidney disease.

4.3. Prevalence of abnormal renal parameters in male and female patients with type 2 diabetes mellitus

Abnormal Creatinine Serum was significantly higher in female (69.6%) compared to male (18.5%) (P ˂0.001). However, no significant differences were reported between male and female according to other abnormal renal parameters, Table 2.

4.4. Prevalence of abnormal renal parameters categorized by patients' glycaemic index

Prevalence of different types of abnormal renal parameters stratified by patients' glycaemic are shown in Table 3. Patients were divided into two groups as per their glycaemic index (HbA1c); the first group consisted of patients with HbA1c ˂ 7.0% and the second group consisted of patients with HbA1c values ≥ 7.0%. Patients with HbA1c values ≥ 7.0% had significantly higher values of Albumin Urine (P = 0.035) and Alb: Cr Ratio (P = 0.011) compared with the patients who had HbA1c ˂ 7.0% Fig. 1.

Table 3
Prevalence of Abnormal renal parameters categorized by patients' glycaemic control.

Parameter	Glycated Haemoglobin (HbA1c) (n = 300)		p. value
	HbA1c < 7 (n = 136)	HbA1c ≥ 7 (n = 164)	
Creatinine Serum mg/dL			
0.72–1.81	83 (47.7%)	91 (52.3%)	0.33
<0.72 & 1.81>	53 (42.1%)	73 (57.9%)	
GFR ml/min			
≥90	110 (47.2%)	123 (52.8%)	0.233
<90	26 (38.8%)	41 (61.2%)	
Albumin Urine mg/L			
≤23	105 (48.8%)	110 (51.2%)	0.035
>23	31 (36.5%)	54 (63.5%)	
Creatinine Urine mg/dL			
37–250	119 (44.7%)	147 (55.3%)	0.562
<37& > 250	17 (50%)	17(50%)	
Alb: Cr Ratio mg/g			
Alb: Cr < 30	114 (49.4%)	117 (50.6%)	0.011
Alb: Cr ≥ 30	22 (31.9%)	47 (68.1%)	

Abbreviations: HbA1c, HbA1c, haemoglobin A1c; GFR, glomerular filtration rate; Alb: Cr, albumin creatinine ratio; p value <

4.5. Abnormal renal profile associated with poorly controlled type 2 diabetes mellitus diabetes (HbA1c ≥ 7)

Table 4 demonstrates the results of logistic regression analysis applied to each abnormal renal parameter. This table shows the results for poorly controlled diabetes mellitus (HbA1c ≥ 7). The odds ratios in this table shows the magnitude of the association and their corresponding p-values indicate whether the association is statistically significant or not by using the cut-off values of 0.05 as mentioned in the method section. In this model poorly controlled diabetes mellitus (HbA1c ≥ 7) were significantly associated with abnormal Albumin Urine (P = 0.034) and abnormal Alb: Cr Ratio (P = 0.011).

Patients with Albumin Urine ˃ 23 mg/L shows 1.66 times of having HbA1c ≥ 7 compared to those with Albumin Urine ≤23 mg/L (95% CI 1.32–2.78). Similarly, patients with Alb: Cr Ratio ≥30 mg/g shows 2 times of having HbA1c ≥ 7 compared to those with Albumin Urine ≤23 mg/L (95% CI 1.18–3.67).

To select the set of factors that jointly influence poorly controlled diabetes mellitus (HbA1c ≥ 7), we used the stepwise procedure applied to the multivariate logistic regression model. The results of this procedure showed that only Alb: Cr Ratio was highly associated with poorly controlled diabetes mellitus (HbA1c ≥ 7) Table 5.

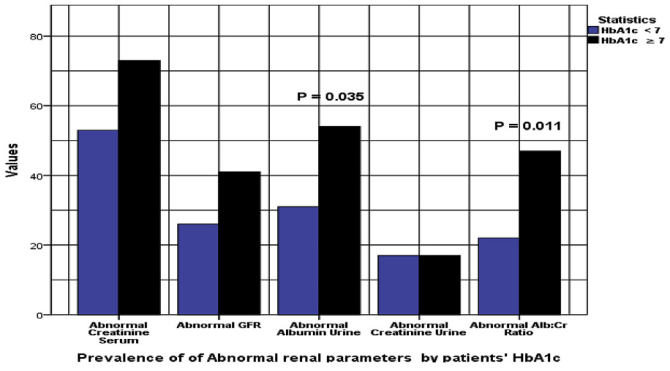

Fig. 1. Bar chart for different types of abnormal renal parameters by patients' HbA1c.

Table 4
Odds ratios of HbA1c ≥ 7 by abnormal renal parameters before and after adjusting for the effect of all other factors.

Abnormal Renal Parameters	HbA1c ≥ 7							
	Unadjusted				Adjusted			
	OR	95% CI		P. value	OR	95% CI		P. value
Creatinine Serum mg/dL (Ref. 0.72–1.81)								
<0.72 & 1.81>	1.26	0.79	1.99	0.33	1.12	0.61	2.07	0.71
GFR ml/min (Ref. ≥ 90)								
<90	1.41	0.81	2.46	0.224	1.369	0.735	2.55	0.32
Albumin Urine mg/L (Ref. ≤ 23)								
>23	1.66	1.32	2.78	0.034	1.456	0.83	2.55	0.19
Creatinine Urine mg/dL (Ref. 37–250)								
<37& > 250	0.81	0.39	1.65	0.56	0.87	0.40	1.90	0.74
Alb: Cr Ratio mg/g (Ref. < 30)								
≥ 30	2.08	1.18	3.67	0.011	1.98	1.112	3.52	0.020

Notes: Adjustment for sex, age, BMI, FBS & vitamin D; P ˂ 0.05 was considered statistically significant.
Abbreviations: OR, odds ratio; CI, confidence interval; HbA1c, hemoglobin A1c; glomerular filtration rate; Alb: Cr, albumin creatinine ratio.

Table 5
Multiple regression analysis for factors associated with poorly controlled diabetes (HbA1c ≥ 7).

Abnormal Renal Parameters	HbA1c ≥ 7			
	OR	95% CI		P. value
Alb: Cr ≥ 30 mg/g	1.92	2.18	3.67	0.001

Abbreviations: OR, odds ratio; CI, confidence interval; HbA1c, hemoglobin A1c; glomerular filtration rate; Alb: Cr, albumin creatinine ratio.

4.6. Vitamin D insufficiency/deficiency associated with chronic kidney disease among patients with type 2 diabetes mellitus diabetes

To investigate the relationship between vitamin D status and chronic kidney disease, a binary logistic regression was used, and the odds ratios shows the magnitude of the association. Chronic kidney disease was significantly associated with D Insufficiency/Deficiency (P = 0.043). Patients with chronic kidney disease more likely to have vitamin D Insufficiency/Deficiency OR (1.765; 95% CI 1.01–3.1). Patients with CKD shows 1.7 times of having vitamin D Insufficiency/Deficiency when compared to those without CKD.

5. Discussion

In our study, from the total number of patients diagnosed with diabetes mellitus type2 a 23% were having chronic kidney disease, correspondingly a previous study concluded a similar prevalence of almost 20% diabetic patients with kidney disease [18], indeed other findings indicated a higher prevalence of diabetic kidney disease in general [19,20]. More specifically for each abnormal renal parameter the percent from the total patients was calculated, serum creatinine, glomerular filtration rate, albumin urine, creatinine urine, albumin: creatinine ratio, 42%, 25.9%, 28.3%, 11.3%, and 23% respectively, obviously patients with abnormal serum creatinine reflect the highest percent, other studies had also examined serum creatinine with diabetic patients and was found to be abnormal, thus patients are recommended to consider cautions for developing kidneys disease in this condition [21]. When we examined the nephropathy status a 77% of the patients was normal (non-nephropathic), 20% was at risk of nephropathy and 9% was diagnosed with nephropathy, in this manner a study had showed a higher percent of diabetic nephropathy almost 20% in Chinese patients [22]. Furthermore, in our patients the occurrence of abnormal renal parameters varies from one patient to another, as 42.78% had one abnormal renal parameter, 16.7% had two and 16.3% had more than two, the presence of more than one abnormal parameter increase the risk of kidney disease progression, with this condition of kidney disease the risk start with the occurrence of one abnormal renal value, then when kidney disease develop to stages more than one abnormal value progress, as mentioned in previous studies [23]. Studies was also considering the use of these clinical tests for not only identification of kidney condition but also management and monitoring [24]. In our study the effect of gender showed a significant difference on renal parameters as female serum creatinine was 69.6% compared to male patients 18.5% (P > 0.001), while the difference with other parameters wasn't significant, still serum creatinine consider as an important biomarker for kidney malfunction, additionally in a gender comparison study of serum creatinine the increase was noticed also in diabetic female patients rather than in male [25]. Other studies also investigated in this means, females were associated with high prevalence of renal dysfunction than male patients [26]. We had divided diabetic patients into two groups regarding glycaemic control according to HbA1c value as un controlled (<or = 7) and controlled (>7) patients, in poor glycaemic control group the number of patients with increased albumin urine and albumin creatinine urine ratio was significant as the P value was (P = 0.035), (P = 0.011) respectively, as clarified by other studies a high ratio of albumin creatinine in type 2 diabetes was indeed occurred with poor blood glucose control [27], in a like manner another study defined the relation between albumin in diabetic patients urine samples and their glycaemic control to be correlated [28]. When adjusting the abnormal renal parameters after the effect of all factors, only abnormal albumin creatinine ratio was a significant value, as it appears to be affected by age or/and weight or/and gender or/and other factors, one example from the literature in this manner is a study determined the variable effect of weight on albumin creatinine ratio in diabetic patients [29]. The last part of our results showed the relation of vitamin D in diabetic patients with chronic kidney disease, the percent of patient was significant whether the vitamin level was deficient or insufficient in these patients (P = 0.043), other studies elaborated on this relation supporting the presence of vitamin D deficiency in addition to a magnitude prevalence in patients with both diabetes mellitus and kidney disease [30,31].

6. Conclusion

This study had revealed a dramatic high prevalence of chronic kidney disease in patients with type 2 diabetes mellitus, while investigating in these patients renal profile the association of

abnormal renal parameters and gender was significantly observed as diabetic female patients was taking over the ratio of abnormal variable, yet patients individualisation is an important criteria in diagnosis, treatment and monitoring. Furthermore, the relation between poor glycaemic controlled patients and the presence of noticeable abnormal values of renal parameters as high albumin and albumin creatinine ratio, indicates the benefit of renal parameters in revealing diabetic status, hence supporting the assessment of kidney function markers in patients with uncontrolled blood glucose level. At last another prevalence was concluded with diabetic patients is the high percent of vitamin D insufficiency/deficiency among patients with chronic kidney disease.

Recommendations: In our study we vividly recommend treatment for diabetic patients with chronic kidney disease and intensive monitoring to delay the progression to advanced stages, in addition correction of vitamin D in these populations could profit in patients' health.

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