Journal of Preventive Epidemiology

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Trends of serum creatinine among patients with type 2 diabetes in Isfahan endocrine and metabolism research center; a longitudinal study

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Received: 7 July 2016
Accepted: 18 Aug. 2016
ePublished: 24 Aug. 2016

Keywords: Diabetes mellitus, Obesity, Albuminuria, Serum creatinine, Triglyceride, Cholesterol

Abstract

Introduction: The increasing rate of prevalence of diabetes in the last 50 years make concerns on the remarkable dangers of diabetes for the population health.
Objectives: Regarding the importance of changing the serum creatinine level over time and limited data and information in Iran about the examining functional changes of creatinine level in diabetic patients, we designed this study for analyzing longitudinal data on serum creatinine.
Patients and Methods: Around 7778 cases, is gathered from suffering diabetes (type 2) and at least two times referral to the department during the survey period. To consider the ethical issues, only the information related to the biological correlation of the patients, without mentioning their name and features, has been used. Variables like sex, age, period of diabetes (the time distant between the diagnosis of the disease and the time of individuals' participation in the survey), the type of treatment (the type of treatment they have achieved when they referred department), fasting blood sugar (FBS), blood urea nitrogen (BUN), body mass index (BMI), cholesterol, triglyceride, systolic blood pressure (SBP) and diastolic blood pressure (DBP) have been considered as independent variables and creatinine as dependent variable.
Results: After modifying time and other variables in the final model, only associations between changes of creatinine level with sex, age, period of diabetes, FBS and BMI remained significant.
Conclusion: This study showed the impact of gender, blood glucose control and weight on renal function and finally its effect on the survival of diabetic patients.

Citation: Hosseini SM, Amini M, Roosta S, Beigrezaei S. Trends of serum creatinine among patients with type 2 diabetes in Isfahan endocrine and metabolism research center; a longitudinal study. J Prev Epidemiol. 2017;2(1):e01.

Introduction

Diabetes mellitus is one of the most prevalent endocrine diseases (1) and is the leading cause of death in the world. Around 90% of diabetic patients are dealing with type 2 diabetes (2-4) and 6% of the world diabetic patients are belongs to Asia. 20% to 30% of adults in some districts of Middle East are stricken with diabetes. The prevalence of diabetes in people older than 40 years in Esfahan is about 7.45% and totally is about 7.8% (3), while diabetes prevalence is 7.4%, 16.3% and 13.5% in Tehran, Yazd and Boushehr, respectively.
The increasing rate of prevalence of diabetes in the last 50 years make concerns on the remarkable dangers of diabetes for the population health (5). It is expected that the prevalence of type 2 diabetes will increase in the future that is caused by increasing the frequency of obesity and less physical activities among people (2).

Core tip
In a-10-year follow up of 7778 diabetic cases, we found only associations between changes of creatinine level with gender, age, period of diabetes, FBS and BMI remained significant.

The prevalence of mellitus diabetes (non-insulin dependent) in Iran was 5.5% in 1995. The World Health Organization (WHO) estimated that it would be 6.8% in 2025, equal to 5 215 000 persons (5).
Around the world, economic expenses of diabetes are remarkable (1). Diabetic patients suffered from major costs and pain (2,3). Epidemiologic studies have shown that diabetic complications in communities are so different from each other (4). One of the most important diabetic complications is the kidney disease. According to the increasing rate of prevalence of diabetes, it is expected that the number of kidney dysfunction cases due to

diabetes will increase significantly in the next century (6). Although all type 2 diabetic patients would not encounter with kidney function disorder, however diabetes and especially type 2 diabetes is the major reason for kidney disease (4,7). On average, 15 years after diagnosis of type 2 diabetes, about 30% of patients will involve by kidney dysfunction (8-11).

Objectives

The blood creatinine test is a method for evaluating kidney function. There is no reference range for the serum creatinine level and each library has its special range. Trend of changing serum creatinine over time is more important than absolute creatinine. A little bit of increase in serum creatinine like 0.2 to 0.8 mg/dL, shows a major deficiency in kidney function (6). Regarding the importance of changing the serum creatinine level over time and limited data and information in Iran about the examining functional changes of creatinine level in diabetic patients, we designed this study for analyzing longitudinal data on serum creatinine.

Patients and Methods

This study is a performing cohort in which the information has been linearly collected. Information gathered in Isfahan Metabolic and Endocrine Research Center. After taking permission and the ethical confirmation, we were allowed to use the information associated to the male and female diabetic patients who have been called on this part during 10 years. This information has been registered in their medical documents. The criterion for entry of samples, which are 7778 cases, is gathered from suffering diabetes (type 2) and at least two times referral to the department during the survey period. To consider the ethical issues, only the information related to the biological correlation of the patients, without mentioning their name and features, has been used. Variables like sex, age, period of diabetes (the time distant between the diagnosis of the disease and the time of person's participation in the survey), the type of treatment (the type of treatment they have achieved when they referred department), fasting blood sugar (FBS), blood urea nitrogen (BUN), body mass index (BMI), cholesterol, triglyceride, systolic blood pressure (SBP) and diastolic blood pressure (DBP) have been considered as independent variables and creatinine as dependent variable.

Ethical issues

1) The research followed the tenets of the Declaration of Helsinki; 2) informed consent was obtained, and they were free to leave the study at any time.

Statistical analysis

The number and the time of patient's references to the center are different. Because of this unbalanced design, the appropriate statistical method is "milled effects model" method which is especially designed for repeated measuring in population survey.

Results

Biological and demographic data of participants have been shown in Tables 1 and 2. Changes of creatinine level over time approximately have a "J" shape (Figure 1).The first analysis showed a significant association between creatinine changes over time, sex, age, period of diabetes, type of treatment, SBP, DBP, BUN, FBS and BMI (Table 3). However, no significant association between changes of creatinine level with cholesterol and triglyceride was found (Table 3). After modifying time and other variables in the final model, only associations between changes of creatinine level with sex, age, period of diabetes, BUN, FBS and BMI remained significant (Table 3).

Discussion

Results of the present showed that changes of creatinine level over time has a second degree trend and approximately has a J shape (Figure 1). Also the results show, a significant association was seen between changes of creat-

Table 1. Demographic data of the patients

Variable	F (%)	Mean ± SD creatinine
Sex		
Female	752 (63.8)	0.89 ± 0.56
Men	426 (36.2)	1.11 ± 0.61
Total	1178 (100)	
Education Level		
Primary and less	852 (72.6)	0.96 ± 0.51
Middle and high	231 (19.6)	0.98 ± 0.63
Academic	92 (7.8)	1.02 ± 0.38
Total	1175 (100)	
Family history of diabetes		
Yes	852 (72.7)	0.96 ± 0.47
No	320 (27.3)	0.98 ± 0.64
Total	1172 (100)	
Type of treatment		
Insulin	155 (33.3)	1.06 ± 0.56
Oral hypoglycemic agents	722 (61.7)	0.94 ± 0.44
Diet	293 (25)	0.98 ± 0.68
Total	1170 (100)	

Table 2 Demographic data of the patients

Variable	Mean ± SD	Variation range	Mid
Duration of diabetes (year)	5.72 ± 5.03	1-20	4
Age (year)	51.98 ± 9.77	3-75	52
BMI (kg/m²)	28.8 ± 4.69	15.6-44.6	28.3
Cholesterol (mg/dL)	215.40 ± 62.42	100-424	211.5
Triglycerides (mg/dL)	211.05 ± 123.64	40-1250	182
Hemoglobin A_1C (g/dL)	8.3 ± 1.87	4.2-14.9	8.1
FBS (mg/dL)	167.03 ± 63.7	50-636	153.5
SBP (mm Hg)	131.74 ± 20.89	70-240	130
DBP (mm Hg)	81.75 ± 10.29	40-130	80
BUN (mg/dL)	26.51 ± 12.95	8-141	25

Abbreviations: FBS, fasting blood sugar; BUN, blood urea nitrogen; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 3. Analysis of the data

	Parameter	Estimated value	CI 95%		SE	t	*P* value
			Low	Top			
Fixed effects	Constant	0.483	0.420	0.546	0.032	14.94	<0.001
	Time	0.001	0.0005	0.002	0.0003	3.82	<0.001
	Time^2	8e-6	4.5e-6	1e-5	2e-6	4.23	<0.001
	Age (years)	0.002	0.0009	0.002	0.0004	4.44	<0.001
	Sex	0.081	0.064	0.099	0.009	9.32	<0.001
	Duration of diabetes (years)	0.003	0.002	0.005	0.0007	4.63	<0.001
	BUN (mg/dL)	0.004	0.0036	0.0044	0.0002	19.2	<0.001
	FBS (mg/dL)	8e-5	1e-5	0.0002	3e-5	2.25	0.025
	BMI (kg/m^2)	0.002	0.0006	0.004	0.0007	2.88	0.004
	Sex & Time	0.0004	-0.0007	-6e-5	0.0002	2.36	0.018
Random effects	SD Constant	0.070	0.059	0.084			
	SD Time	0.0008	0.0006	0.001			
	Remaining	0.106	0.058	0.118			
	ρ	0.139	0.058	0.218			

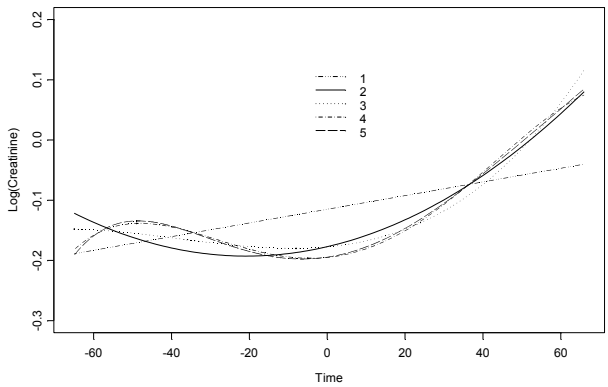

Figure 1. Changes of creatinine level overtime approximately have a "J" shape.

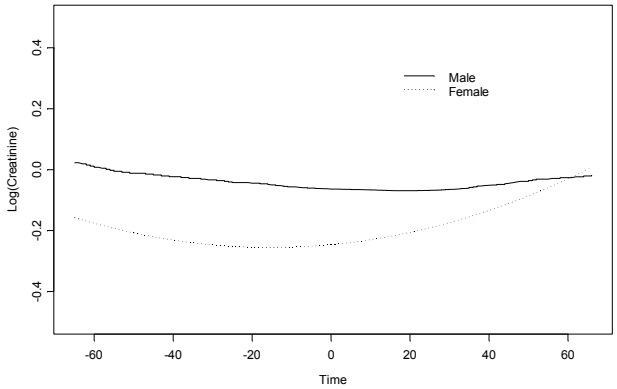

Figure 2. Serum creatinine level in men is higher than women after passing about 10 years from starting the study (*P* = 0.01).

inine level over time with sex. As it is shown in Figure 2, the serum creatinine level in men is higher than women after passing about 10 years from starting the study. Similarly in subsequent studies conducted by Retnakaran et al and Kremp, in type 2 diabetes patients, men gender is a risk factor for nephropathy and albuminuria (7,12). As it is shown in Table 3, the creatinine level over time has a significant association with age. Other studies also mentioned that age is a significant risk factor for chronic kidney disease (13-16). Our results show that, increasing the period of diabetes was associated with increasing creatinine level significantly. Similarly Narenpitak and Narenpitak, in their study found that the risk of diabetic nephropathy and the final stage of kidney disease increase as diabetic period increases (17-27).

In our study a significant association between changes of creatinine level over time and level of BUN was seen. This result was similar to the study of Cauthen et al, which revealed a significant association between creatinine and level of BUN (28). Daniel also showed an association between kidney function disorder and high level of BUN (29).

In this study there was a significant association between changes of creatinine level over time and BMI. Studies of Ravid et al, Bruno et al, Gelber et al and Hsu et al, showed the risk of kidney with increasing the BMI (30-33).

In the first analysis of trend changes in creatinine with triglyceride and cholesterol serum values, no significant association was seen. Thomaseth et al, in their longitude study found no significant association between changes of glomerular filtration rate (GFR) with triglyceride and cholesterol serum values in type 2 diabetic patients over time (34). Also in the study conducted by Sigdel et al, triglyceride and cholesterol were not significant risk factors for albuminuria (35-37). Early analyses showed significant association between changes of creatinine level, type of treatment, systolic and diastolic blood pressure; but after modifying other variables in the final model these associations were not meaningful. In line with our study results, Leehey et al in the cohort of diabetic patients with chronic kidney disease, concluded that systolic and diastolic blood pressure has an association with the progress of kidney disease in the one variable analyses, but in multivariable analyses this association was not meaningful (6). Contrary to our study results, in some studies systolic blood pressure and diastolic blood pressure were risk factors for kidney disease (7,12,14,30,38,39). Some other studies reported that triglyceride and cholesterol were potential risk factors for kidney disease (7,30-33,36,37).

Similarly Ravid et al in their study showed that, the type of treatment including diet, oral drugs/medicine or insulin are not exactly a potential risk factor for kidney disease (30). Also Bronu et al in their study of cohort utilizing type 2 diabetic patients, concluded that the risk of chronic kidney disease in patients who take oral medicine is about 1.4 times more than patients who follow diet and this risk in patients who have insulin is about 2.26 times more than diet (31).

Limitations of the study

Small proportion of the patients was a limitation of our investigation.

Authors' contribution

All authors contributed to design of the research. All authors read, revised, and approved the final manuscript.

Conflict of interests

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

Funding/Support

This study was financially supported by Isfahan University of Medical Sciences.

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