

# Trends of diabetic nephropathy prevalence in Isfahan, Iran, during 1992-2010

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**Background:** Diabetes mellitus is a metabolic disorder and its subsequent complications such as retinopathy, nephropathy, ulcers, disability, and amputation increase the burden of the disease. Patient knowledge-improving programs are employed to prevent disease progression and to improve the quality of life of the patients. In this way, we need to characterize the groups of patients in urgent need for more and rich-in-content programs. In the present study, we used piecewise regression to evaluate the trends of diabetic nephropathy prevalence in patients registered in the Sedigheh-Tahereh Research Center and to identify patients who were in need of more attention. **Materials and Methods:** Piecewise regression, used in this study, is a statistical method to identify change points, if any, in the trends of mortality rates, prevalence of a disease, or any other trends. Available information for 1,935 patients were retrieved from the database. Joinpoint program 3.5.3 and Statistical Package for the Social Sciences (SPSS) 20 was used to fit piecewise regression and obtain descriptive statistics, respectively. **Results:** We assessed the trend of diabetic nephropathy in different groups of diabetic patients with respect to sex, blood pressure status, education, family history of diabetes, and age. The results showed an increasing trend in females, patients without family history of diabetes, and over the recent years. The prevalence of diabetic nephropathy in patients with academic education was high. **Conclusion:** The groups with high prevalence or increasing trends need more preventive intervention and detailed assessment of the present trends. Exploring high-risk groups is beneficial for better policy-making in the future. However, discovering the reasons for the increased trend of the disease is really helpful in controlling diabetes complications.

**Key words:** Diabetic nephropathy, piecewise regression, prevalence, trend

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## INTRODUCTION

Diabetes is the fifth common cause of death due to diseases in the United States and is considered as the fourth cause of referring to physicians.<sup>[1,2]</sup> Diabetes mellitus is a metabolic disorder characterized by hyperglycemia with metabolic disturbances as a result of defects in insulin secretion, insulin action, or both.<sup>[3,4]</sup> Accumulation of glucose in the serum could have different effects on health and quality of life. Long-term damage and dysfunctional organs are its consequences. The risk of cardiovascular and renal disorders is 2 times and 17 times greater in these patients. One-third of new cases of

kidney disorders arise in diabetic patients.<sup>[1,5]</sup> Mortality rates in diabetic patients are 1.5-2.5% greater compared to healthy people; their survival is 10-15 years shorter than the general population, and the costs of a diabetic patient is 3.8 times higher than other patients.<sup>[5]</sup> As a health issue, diabetes lowers the quality of life of the patients.

Progressive complications of diabetes such as retinopathy with blindness and nephropathy could lead to renal failure, neuropathy, diabetic foot ulcers, and amputation.<sup>[3,4]</sup> Diabetic nephropathy is the first cause of chronic kidney disease (CKD), which results in end-stage renal disease (ESRD) and early death in both developing and developed countries and its mortality rate is high. Excess mortality rate in diabetic patients is

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almost through kidney diseases such that the mortality rate in these patients is similar to the general population in the absence of renal disorders.<sup>[6,7]</sup>

Incidence rate of kidney diseases depends on factors such as type of diabetes, management of diabetes including blood glucose and blood pressure control, and occurring cardiovascular disorders. Hypertension, age, hyperglycemia, race, smoking, diabetes duration, poverty, and genetic backgrounds are the most important risk factors of renal disorders in diabetic patients.<sup>[6,8]</sup>

Glomerular filtration rate (GFR) is used as a criterion to assess renal diseases. In a normal person, its range is higher than 90 mL/min/1.73 m<sup>2</sup>.<sup>[9]</sup> Lower values indicate renal disorders, which are categorized into four stages, namely, GFR 60-89, 30-59, 15-29, and <15 mL/min/1.73 m<sup>2</sup>, which are defined as mildly, moderately, severely, and very severely reduced kidney function, respectively.

Diabetes is a costly disease and several studies have been performed to estimate its social and economic burdens.<sup>[1,2,5]</sup> Determination of the trend of diseases and its changes synchronically may have an important role in evaluating the success of disease control strategies, health development indicators, and health planning. Due to the importance of incidence trends of renal disorders in diabetic patients, we studied the trends of renal disorders in type 2 diabetic patients registered in the Sedigheh-Tahereh Endocrinology and Metabolism Research Center from 1992 to 2010 using piecewise regression models. Despite linear regression models, this model reveals the breakpoints in the trend and provides estimates of the slope in each piece.

## MATERIALS AND METHODS

The database of the Sedigheh-Tahereh Endocrinology and Metabolism Research Center was used to extract demographic and characteristic information of type 2 diabetes patients registered in this center. Each person was diagnosed as diabetic if his/her fasting blood sugar was higher than 126 mg/dL and 2-h plasma glucose concentration was higher than 200 mg/dL.<sup>[3]</sup> The available data from 1992 to 2010 was used. For these patients, data on the variables of sex, age, education, family history of diabetes, blood pressure, and estimated glomerular filtration rate (eGFR) were retrieved from the database. The eGFR, which is calculated using Modification of Diet in Renal Disease (MDRD) formula based on serum creatinine level was used to define the stage of chronic kidney disease. According to the National Institute of Diabetes and Digestive and Kidney Diseases, an estimated GFR below 60 mL/min per 1.73 m<sup>2</sup> for at least 3 months was considered to be a chronic kidney disease.

In this database, patients with systolic blood pressure higher than 135 mmHg and diastolic blood pressure higher than 85 mmHg were considered to have hypertension.<sup>[10]</sup> Education was classified to with and without academic education.

The proportion of patients at different levels of eGFR was considered as the dependent variable and the successive number of years served as the independent variable. In each year, the study population was divided into different categories according to the levels of the variables of interest and the year or years in which the change point had been occurred was determined. Then, the results for these categories were compared.

We used piecewise regression to study the trends of renal disorders. Piecewise regression is a statistical technique for determining change points in the trends of mortality or incidence rates. In this method, models with different change points are fitted and various points are assessed and the change points are determined on the basis of the fitness criteria. This method extends to the situation with nonconstant variance and possibly autocorrelated errors. Various methods have been proposed and used for finding the change points in the literature.<sup>[11,12]</sup>

This method is implemented in different statistical packages. We used Joinpoint Regression Program 3.5.3 (National Cancer Institute) to explore change-point years in which the proportion of patients with certain levels of eGFR changes its trend.<sup>[13]</sup> This software has been used in various studies.

As a number of years we considered a maximum of three join points (four distinct temporal trends), and used the Monte Carlo permutation method to assess significant changes in time trends. The results were considered to be significant at 0.05 levels.<sup>[11]</sup>

The prevalence trends of renal disorders in type 2 diabetic patients were assessed with respect to various variables of interest and the results of the best fit among competing models are presented below. Due to the low proportion in some categories of the variables, the level of eGFR suggesting the renal disorder was considered to be different for different variables. For the variables sex, blood pressure, and age when we defined level of 30 mg/dL for eGFR as the disorder threshold, there was an adequate number of patients each year and the resulting graph was reasonable. For the variables education and family history, this threshold was considered to be 60 mg/dL.

## RESULTS

A total of 1,935 patients were included in the study, out of which 37.2% were males and 62.8% were females. Of the

patients 35% had high blood pressure (BP) at their first visit. In this population, only 12.5% had academic education and 73.6% of the patients had a reported family history of diabetes.

Figure 1 shows the results for the variable sex. The number at the top of figure refers to the number of break points for the best model. In females, the proportion of patients with eGFR less than 30 mg/dL had a decreasing trend up to significant change in the year 1996 ( $P$  value = 0.01). Thereafter, the trend was stable until 2008 where it became slightly increasing ( $P$  value = 0.06). The trend was decreasing without any change point in males.

In patients with hypertension, the trend was decreasing up to 1997 where a change point occurred and it became stable as shown in Figure 2a. The trend was steadily decreasing among patients with normal blood pressure [Figure 2b].

To evaluate the trends with respect to age, we categorized age as <30 years, 30-40 years, 40-50 years, 50-60 years, 60-70 years, and >70 years. The trend was decreasing without any change in the pattern in categories <30 years and 30-40 years as shown in Figures 3a and b. However, the rate of decline was higher for <30 year-old age group. As Figure 3c. shows that for the age group 40-50 years, the trend was slightly increasing after 1997. The trend was almost fixed for the age group of 60-70 years [Figure 3e]. Both the age groups of

50-60 years and >70 years experienced a decreasing pattern with a change point at 1996 and 1997, respectively. However, for the age group of 50-60 years, the trend was fixed after the change point but it was increasing for age group of >70 years as shown in Figures 3d and f.

From Figure 4a, it can be inferred that the trend was roughly increasing in patients without diabetic relatives over the study period. But the situation was different in patients with diabetic family members. As shown in Figure 4b, the trend for this group was increasing up to 2007 but tended to go downward after that.

The trend was increasing for both education levels but the rate of increase was almost three times steeper for patients with academic education [Figures 5a and b].

## DISCUSSION

The management of diabetes complications mainly centers around the control of plasma glucose and blood pressure.<sup>[7,14]</sup> Microalbuminuria is an onset indicator of diabetic nephropathy, which occurs more in patients with elevated blood pressure.<sup>[15]</sup> Our study suggests that blood pressure control has been successful, as the proportions of renal complications in patients with hypertension at the first visit were fixed after 1997. The results also show a declining trend of renal complications in both genders after 1996. A slight increasing pattern is present in women, however.

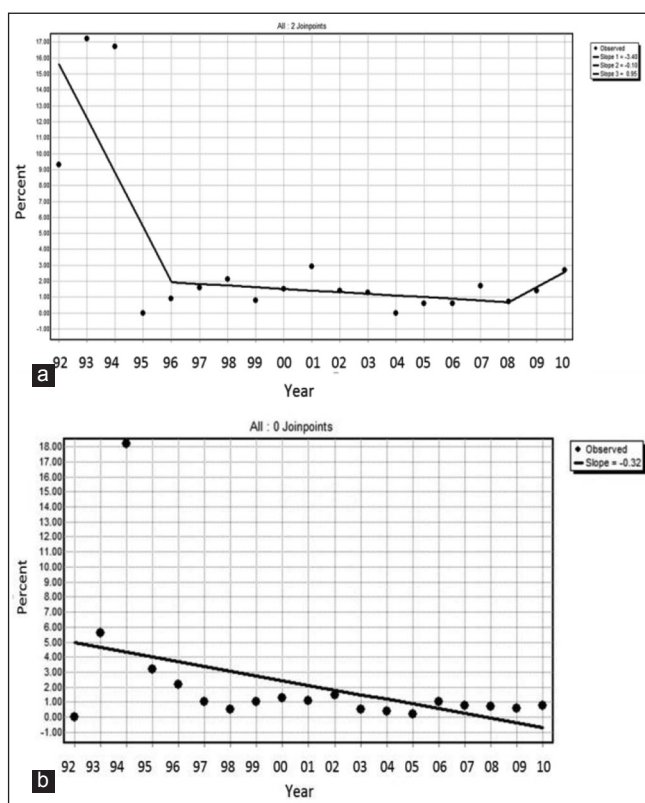


Figure 1: Trends for (a) females (b) males

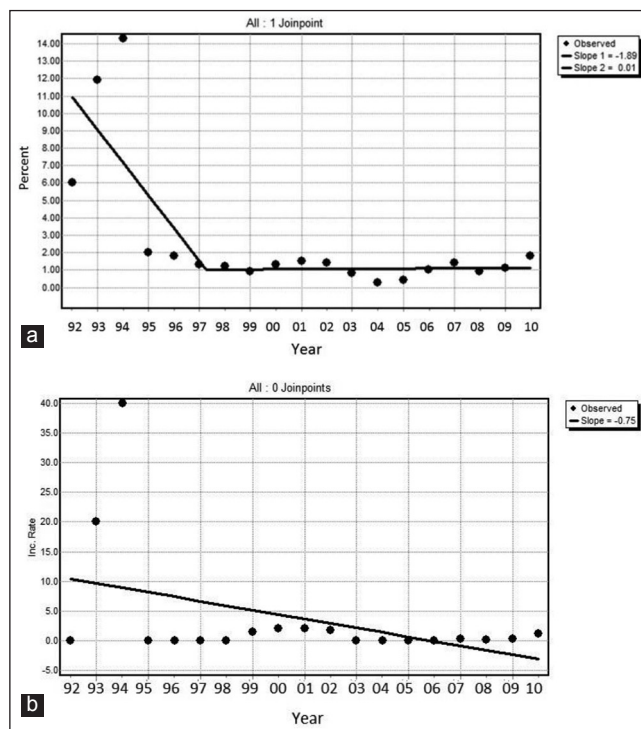


Figure 2: Trend for patients (a) with hypertension (b) without hypertension

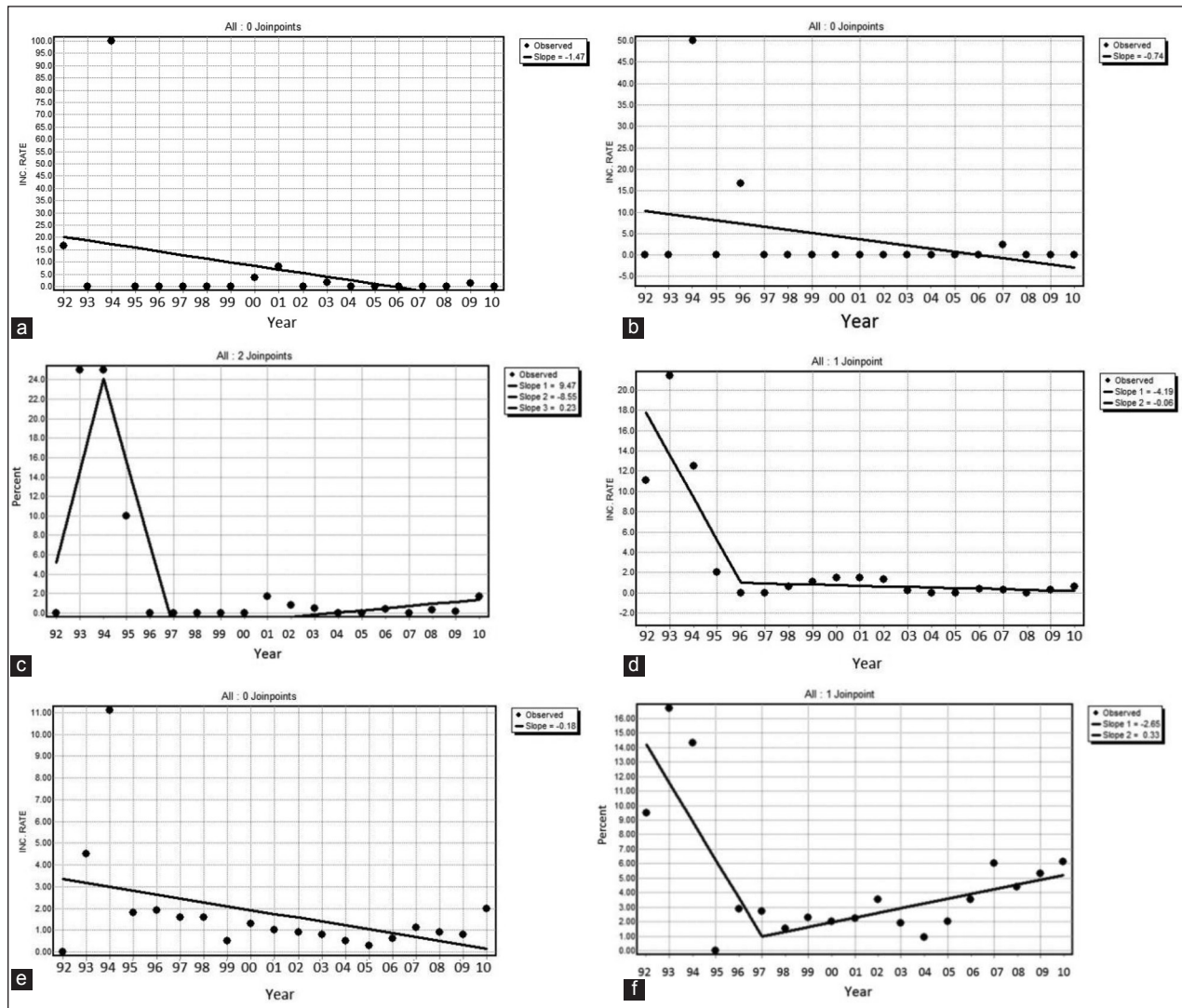


Figure 3: Trends for the age group (a) <30 years (b) 30-40 years (c) 40-50 years (d) 50-60 years (e) 60-70 years (f) >70 years

Janmohamed *et al.* reported that there was a direct relationship between age and the renal disorders in diabetic patients.<sup>[16]</sup> De Boar *et al.* reported that between 1998 to 2008, there was an increasing trend of prevalence in diabetic renal disease in the US population; furthermore, the increasing trend was most for the age group of >65 years.<sup>[17]</sup> Our study showed that the rate of renal disorders in these patients had a decreasing trend except for the age group of >70 years in which the trend was increasing. This indicates that this group needs more care to control renal disorders. Lifestyle changes and an increasing pattern of chronic diseases, especially cardiovascular diseases in the elderly, additionally low awareness of the condition in younger people may explain such a trend in this group.<sup>[18]</sup> Studies reported an overall awareness rate of renal disorders of 9.7% and 3.5% for stages 3-5 and 1-5, respectively.<sup>[19]</sup> The increasing proportion of the elderly in Iran has increased the number of patients at risk of diabetic nephropathy. Improvements in public health and medical care have

prolonged life expectancy and created an upward trend of the elderly population in Iran between 1999 and 2011 for the age group of >65 years.

The different results among studies might have been due to the specific regions that were studied. Studies indicated the disparity in health care between areas with different socioeconomic status.<sup>[20]</sup>

The proportion of stage 2 renal disorders in patients with family history of diabetes was declining up to 2004 but increased after this year with a slope of 5.16 until 2007. A similar pattern was seen in patients without family history of diabetes. These results are consistent with previous studies.<sup>[21]</sup> Ahmad *et al.* reported an odds ratio of 1.23 for diabetic nephropathy in patients with family history of diabetes.<sup>[22]</sup> Although a family history of diabetes is considered to be a risk factor for developing renal disease, these results indicated that family history

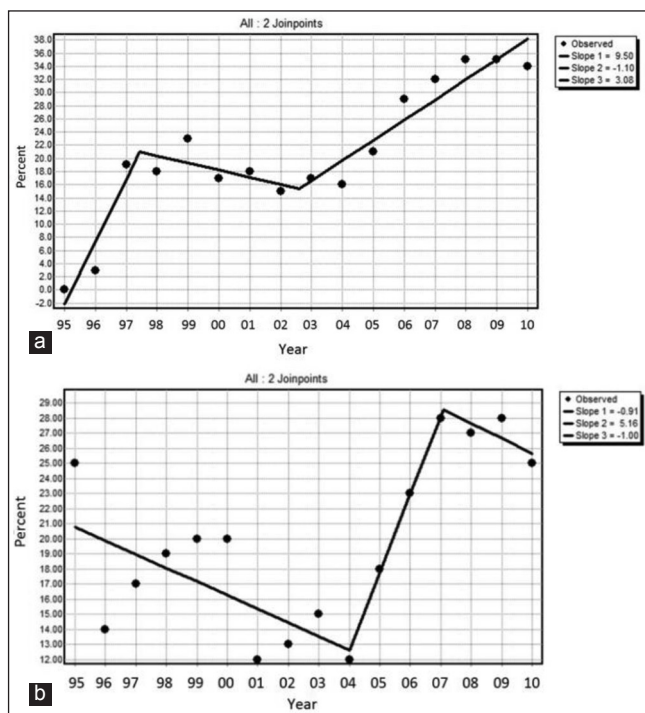


Figure 4: Trend for (a) patients without diabetic family members (b) patients with diabetic family members

does not influence the trend of renal disorders for this population.<sup>[23]</sup> Our study revealed better management of renal disorders in patients with family history of diabetes than the other patients. In this group, the trend was decreasing and the prevalence in recent years was almost 25% while the trend was ascending in the other groups with prevalence of more than 30% in the recent years. The trend of renal complications was increasing among patients with academic education.

In general, the results suggest that more attention is required in terms of improving patients' knowledge and putting more preventive programs into action, especially for women and elderly patients. An increasing rate of renal disorders in patients without family history of diabetes suggests that the educational and preventive programs have not been efficient.

Finding the reasons of the present trends in patients with academic education could be instructive. Perhaps reasons such as lifestyle and stress are responsible for an increasing trend in this group.

This study tries to reflect the current trends of renal disorders with respect to various patient characteristics. However, it does not explore potential reasons and risk factors affecting these trends and does not determine whether the shortcomings are present in patient knowledge-elevating programs or the trends are affected by the other sources. Undoubtedly, expanding patient knowledge about

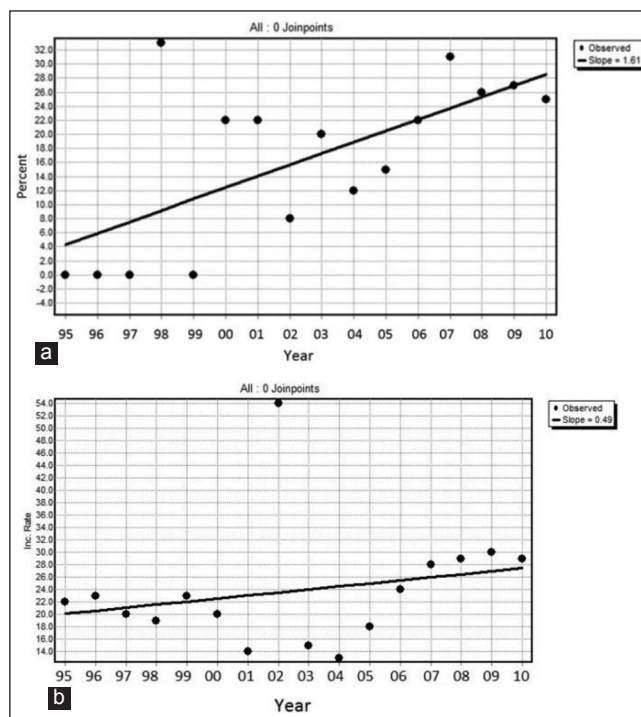


Figure 5: Trend for patients (a) with (b) without academic education

diabetes, its treatment, and lifestyle modifications would be helpful in the delayed onset and slow progression of its subsequent complications.

## CONCLUSION

Studying the trends of a disease helps in evaluating previous health and treatment programs and formulating new hypotheses for future researches. In this study, we assessed various groups of patients and specified those groups with increasing patterns of diabetic nephropathy that need more research to determine the factors related to these patterns.

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## Conflicts of interest

The authors have no competing interests.

## AUTHOR'S CONTRIBUTION

All authors contributed in the conception of the work, conducting the study, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work.

## REFERENCES

1. Sadeghi Mazidi A, Kharazmi E, Javanbakht M, Heidari A, Bayati M. Economics cost of diabetes in type II diabetic patients. *Payesh* 2012;11:443-9.
2. Tol A, Tavassoli E, Sharifirad G, Shojaezadeh D, Azadbakht L. The relationship between socioeconomic factors and their effects on patients with type 2 diabetes. *Health Sys Res* 2010;7:1-10.
3. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. *Diabet Med* 1998;15:539-53.
4. WHO Consultation Definition, diagnosis and classification of diabetes mellitus and its complications. Geneva, Switzerland: World Health Organization 1999. p. 1-59.
5. Amini M, Khadivi R, Haghighi S. Costs of type 2 diabetes in Isfahan-Iran in 1998. *J Diabetes Metab Disord* 2002;4:97-104.
6. Thompson CS. Diabetic nephropathy: Treatment with phosphodiesterase type 5 inhibitors. *World J Diabetes* 2013;4:124-9.
7. Himmelfarb J, Tuttle KR. New therapies for diabetic kidney disease. *N Engl J Med* 2013;;369:2549-50.
8. Shao H, Song C, Xu D, Shang X, Hao Z. Analyses on the relative factors regarding diabetic nephropathy. *Zhonghua Liu Xing Bing Xue Za Zhi* 2013;34:393-5.
9. Edelstein CL. Biomarkers of Kidney Disease. Academic Press; 2011.
10. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo Jr JL, *et al.*; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: The JNC 7 report. *JAMA* 2003;289:2560-72.
11. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med* 2000;19:335-51.
12. Arsang S, Kazemnejad A, Amani F. Applying Segmented Regression Model to Analysis the Trend of Tuberculosis Incidence Rate in Iran Between 1964-2008. *Iranian J Epidemiol* 2011;7:6-12.
13. Joinpoint Regression Program. Statistical Research and Applications Branch, National Cancer Institute; 2012.
14. Yang Y, Land KC. A mixed models approach to the age-period-cohort analysis of repeated cross-section surveys, with an application to data on trends in verbal test scores. *Sociol Methodol* 2006;36:75-97.
15. Al-Agha A, Ocheltree A, Hakeem A. Occurrence of microalbuminuria among children and adolescents with insulin-dependent diabetes mellitus. *Saudi J Kidney Dis Transpl* 2013;24:1180-8.
16. Janmohamed MN, Kalluvya SE, Mueller A, Kabangila R, Smart LR, Downs JA, *et al.* Prevalence of chronic kidney disease in diabetic adult out-patients in Tanzania. *BMC Nephrol* 2013;14:183.
17. de Boer IH, Rue TC, Hall YN, Heagerty PJ, Weiss NS, Himmelfarb J. Temporal trends in the prevalence of diabetic kidney disease in the United States. *JAMA* 2011;305:2532-9.
18. Zhang L, Wang F, Wang L, Wang W, Liu B, Liu J, *et al.* Prevalence of chronic kidney disease in China: A cross-sectional survey. *Lancet* 2012;379:815-22.
19. Hsu CC, Hwang SJ, Wen CP, Chang HY, Chen T, Shiu RS, *et al.* High prevalence and low awareness of CKD in Taiwan: A study on the relationship between serum creatinine and awareness from a nationally representative survey. *Am J Kidney Dis* 2006;48:727-38.
20. Yang W, Lu J, Weng J, Jia W, Ji L, Xiao J, *et al.*; China National Diabetes and Metabolic Disorders Study Group. Prevalence of diabetes among men and women in China. *N Engl J Med* 2010;362:1090-101.
21. Freedman BI, Soucie JM, McClellan WM. Family history of end-stage renal disease among incident dialysis patients. *J Am Soc Nephrol* 1997;8:1942-5.
22. Ahmed MA, Kishore G, Khader HA, Kasturirangan MN. Risk factors and management of diabetic nephropathy. *Saudi J Kidney Dis Transpl* 2013;24:1242-7.
23. National chronic kidney disease fact sheet: General information and national estimates on chronic kidney disease in the United States. Centers for Disease Control Prevention, 2010.