

Changing Epidemiology of End-Stage Renal Disease in Last 10 Years in Iran

Mohammad Aghighi,¹ Mitra Mahdavi-Mazdeh,² Mahnaz Zamyadi,¹
Alireza Heidary Rouchi,¹ Hamid Rajolani,¹ Shahram Nourozi¹

¹Center of Transplantation and Special Diseases, Ministry of Health, Tehran, Iran

²Division of Nephrology, Department of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Keywords. Chronic kidney failure, dialysis, Iran, epidemiology

Introduction. The rapid increase in the prevalence of end-stage renal disease (ESRD) necessitates putting into practice some strategies to prevent its development and progression, especially in the developing world. Detailed chronological changes in the incidence of ESRD may sharpen the focus on its prevention. We, therefore, determined the detailed epidemiological features of ESRD in Iran. **Materials and Methods.** Data of the national registry of Iran's ESRD provided by the Ministry of Health were used to retrieve the ESRD figures between 1997 and 2006.

Results. A total of 35 859 patients who initiated renal replacement therapy (20 633 men and 15 226 women) were registered during the study period from 1997 to 2006. The annual number of patients with ESRD beginning maintenance treatment in Iran increased 130% between 2000 and 2006. During 1997 to 2006, the proportion of new cases of ESRD attributed to diabetes mellitus increased 2-fold from 16% in 1997 to 31% in 2006. The mean age of newly registered men and women increased from 47.0 years and 49.0 years to 52.5 years and 53.0 years, respectively. As for all and major causes of ESRD, age-adjusted incidence rates for men generally were higher than those for women. Male-female ratio was 1.3:1, with no significant changes during this period.

Conclusions. We strongly recommend considering chronic kidney disease prevention with initial focusing on strategies and treatment modalities that slow ESRD progression in order to postpone the need for renal replacement therapy.

IJKD 2009;3:192-6
www.ijkd.org

INTRODUCTION

End-stage renal disease (ESRD) is a costly and disabling condition associated with a high mortality rate. The number of patients with ESRD globally continues to grow at an unexpected rate, and greater than the yearly world population growth rate.¹⁻³ Ninety percent of patients with ESRD live in high-income countries, where the average gross income is in excess of US \$ 10 000 per capita.⁴ It is apparent that the prevalence

is largely a matter of survival made possible by renal replacement therapy (RRT), which, in turn, is dependent on healthcare expenditures and economic strength. The prevalence of ESRD in the United States and the European Union is 1500 and about 800 per million population (pmp), respectively.

In developing countries, the figures vary from less than 100 pmp in sub-Saharan Africa and India to about 330 pmp in Jordan, 360 pmp in Iran, and

more than 600 pmp in Saudi Arabia.¹⁻³ The number of patients accepted in the dialysis program is about 80 pmp in Egypt, 20 pmp in Malaysia, and even lower in many other countries. Less than 10% of all patients with ESRD receive any kind of RRT in countries such as India and Pakistan.⁴ Thus, the rapid increase in the prevalence of ESRD and the enormous cost of treatment necessitates urgent approach to implement strategies to prevent development and progression of ESRD, especially in the developing world. Detailed chronological changes in the incidence of ESRD may sharpen the focus on its prevention. We, therefore, determined the detailed epidemiological features of ESRD in Iran by examining the trends in age-specific incidence rates by gender and cause using the data from a nationwide patient registry.

MATERIALS AND METHODS

The national registry of Iran's ESRD is maintained by the Ministry of Health (MOH). As all patients on maintenance RRT are entitled to a government subsidy, transplantation and dialysis units in the country have to report new patients and changes in their treatment modality to the MOH. In each case, the attending nephrologists or internists determine the primary diagnosis. Therefore, registrations are believed to have been sufficiently complete. The important methodological issue which needs elucidation is that some patients with ESRD might not have undergone RRT, and for that reason we may have underestimated the ESRD incidence.

We retrieved demographic data, age, and the primary diagnosis of ESRD during the past 10 years (1997 to 2006). All the analyses were conducted using the SPSS software (Statistical Package for the

Social Sciences, version 14.0, SPSS Inc, Chicago, Ill, USA). Descriptive statistics were used to characterize variables.

RESULTS

A total of 35 859 patients who initiated RRT (20 633 men and 15 226 women) were registered during the study period from the beginning of 1997 through to the end of 2006. Male-female ratio was 1.3:1, which had no significant changes during this period. The annual number of patients beginning maintenance RRT in Iran increased 130% from 2000 to 2006. The incidence rate of ESRD linearly increased from 13.82 pmp in 1997 to 49.9 pmp in 2000 and to 63.8 pmp in 2006.

The findings indicated that from 1997 to 2006, the percentage of new patients with ESRD, attributed to diabetes mellitus increased 2-fold from 16% in 1997 to 31% in 2006. The incidence of ESRD due to hypertension fluctuated, but did not change significantly (roughly 21%). The comprehensive data of ESRD causes and the different slopes of their changes during each year of the study period are summarized in Figure 1.

The mean age of men and women diagnosed with ESRD increased from 47.0 years and 49.0 years to 52.5 years and 53.0 years, respectively. The detailed changes of age and sex during each year of the study period are summarized in the Table and Figure 2. As for all and major causes of ESRD, age-adjusted incidence rates for men generally were higher than those for women. Diabetic nephropathy and possibly hypertensive nephrosclerosis were the leading causes of ESRD in Iran. The rate of ESRD due to unknown causes was more than 20% in all the studied years.

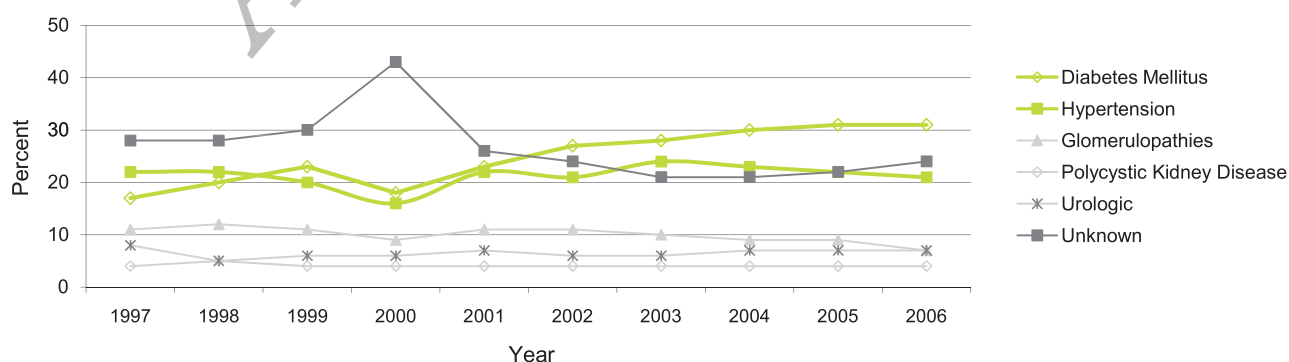


Figure 1. Causes of end-stage renal disease between 1997 and 2006.

Age-Specific Percentages of End-stage Renal Disease in Iran

| Year | Age, y | | | | | | | | | | | | Missing |
|-----------|--------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|------|---------|
| | < 25 | 25 to 29 | 30 to 34 | 35 to 39 | 40 to 44 | 45 to 49 | 50 to 54 | 55 to 59 | 60 to 64 | 65 to 69 | 70 to 74 | >74 | |
| 1996-97 | | | | | | | | | | | | | |
| Male, % | 12.9 | 8.6 | 5.3 | 6.3 | 8.6 | 5.9 | 9.2 | 11.9 | 13.1 | 8.8 | 6.3 | 2.6 | 0.4 |
| Female, % | 7.2 | 5.1 | 5.4 | 8.3 | 10.3 | 11.4 | 10.7 | 15 | 11.9 | 8.5 | 4.9 | 1.3 | 0 |
| Total, % | 10.2 | 6.9 | 5.3 | 7.3 | 9.4 | 8.5 | 9.9 | 13.4 | 12.5 | 8.7 | 5.7 | 2 | 0.2 |
| 1997-98 | | | | | | | | | | | | | |
| Male, % | 8.8 | 6.2 | 5.8 | 4.8 | 7.1 | 8.6 | 10.9 | 11.3 | 14.1 | 10.6 | 8.1 | 3.3 | 0.3 |
| Female, % | 12.0 | 4.8 | 5.9 | 8.0 | 8.4 | 10.6 | 11.6 | 9.8 | 11.3 | 9.7 | 5.7 | 2.0 | 0.3 |
| Total, % | 10.3 | 5.6 | 5.9 | 6.3 | 7.7 | 9.5 | 11.2 | 10.6 | 12.8 | 10.2 | 7 | 2.7 | 0.3 |
| 1998-99 | | | | | | | | | | | | | |
| Male, % | 10.4 | 7.0 | 6.5 | 7.1 | 8.7 | 10.0 | 7.7 | 9.7 | 12.6 | 9.0 | 6.7 | 3.9 | 1.0 |
| Female, % | 10.6 | 5.7 | 6.6 | 5.7 | 7.1 | 9.2 | 10.8 | 11.4 | 11.1 | 11.4 | 6.9 | 3.1 | 0.7 |
| Total, % | 10.3 | 6.4 | 6.5 | 6.5 | 8.0 | 9.6 | 9.0 | 10.4 | 12.0 | 10.0 | 6.7 | 3.4 | 0.9 |
| 1999-2000 | | | | | | | | | | | | | |
| Male, % | 10.9 | 5.2 | 5.7 | 6.3 | 8.4 | 9.3 | 9.2 | 9.0 | 11.6 | 11.0 | 5.9 | 6.2 | 1.3 |
| Female, % | 11.9 | 5.6 | 5.2 | 6.1 | 7.4 | 8.9 | 9.3 | 10.7 | 12.7 | 9.9 | 7.2 | 3.6 | 1.3 |
| Total, % | 11.3 | 5.3 | 5.5 | 6.3 | 8.0 | 9.1 | 9.2 | 9.7 | 12.1 | 10.6 | 6.4 | 5.2 | 1.3 |
| 2000-01 | | | | | | | | | | | | | |
| Male, % | 11.2 | 5.9 | 6.0 | 6.1 | 7.3 | 10.1 | 9.8 | 8.5 | 9.5 | 10.8 | 8.2 | 6.3 | 0.5 |
| Female, % | 11.6 | 4.8 | 6.1 | 5.3 | 6.7 | 9.9 | 10.5 | 9.2 | 10.7 | 11.5 | 7.9 | 5.3 | 0.7 |
| Total, % | 11.4 | 5.4 | 6.0 | 5.8 | 7.0 | 10.0 | 10.1 | 8.8 | 10.0 | 11.1 | 8.1 | 5.8 | 0.6 |
| 2001-02 | | | | | | | | | | | | | |
| Male, % | 11.1 | 5.0 | 6.6 | 5.9 | 7.5 | 9.0 | 9.2 | 8.2 | 9.1 | 11.2 | 8.4 | 8.5 | 0.3 |
| Female, % | 11.3 | 4.4 | 5.6 | 5.3 | 7.1 | 8.7 | 9.6 | 11.0 | 11.5 | 9.8 | 7.8 | 7.3 | 0.7 |
| Total, % | 11.1 | 4.8 | 6.2 | 5.7 | 7.3 | 8.9 | 9.4 | 9.4 | 10.1 | 10.6 | 8.2 | 8.1 | 0.4 |
| 2002-03 | | | | | | | | | | | | | |
| Male, % | 12.2 | 5.9 | 5.5 | 5.0 | 6.9 | 9.0 | 8.8 | 9.4 | 9.0 | 10.6 | 8.3 | 8.3 | 1.3 |
| Female, % | 11.4 | 4.5 | 5.6 | 4.9 | 6.8 | 8.6 | 10.0 | 11.9 | 10.8 | 9.9 | 6.8 | 7.5 | 1.4 |
| Total, % | 11.8 | 5.3 | 5.5 | 4.9 | 6.9 | 8.8 | 9.3 | 10.5 | 9.7 | 10.3 | 7.7 | 8.0 | 1.3 |
| 2003-04 | | | | | | | | | | | | | |
| Male, % | 10.1 | 5.3 | 4.8 | 5.2 | 7.4 | 8.2 | 10.3 | 9.8 | 9.2 | 9.6 | 9.1 | 9.1 | 2.0 |
| Female, % | 10.6 | 3.9 | 4.9 | 5.7 | 5.8 | 9.1 | 11.1 | 11.1 | 10.5 | 10.4 | 9.2 | 5.5 | 2.1 |
| Total, % | 10.4 | 4.7 | 4.8 | 5.4 | 6.7 | 8.6 | 10.6 | 10.4 | 9.8 | 9.9 | 9.2 | 7.4 | 2.0 |
| 2004-05 | | | | | | | | | | | | | |
| Male, % | 8.1 | 5.3 | 4.9 | 4.8 | 6.2 | 8.2 | 11.1 | 9.7 | 9.6 | 10.1 | 9.8 | 10.0 | 2.2 |
| Female, % | 9.8 | 3.8 | 4.6 | 4.1 | 5.9 | 7.9 | 10.2 | 10.2 | 10.9 | 11.0 | 9.9 | 9.0 | 2.8 |
| Total, % | 8.9 | 4.6 | 4.8 | 4.5 | 6.1 | 8.1 | 10.7 | 9.9 | 10.1 | 10.5 | 9.8 | 9.5 | 2.5 |
| 2005-06 | | | | | | | | | | | | | |
| Male, % | 8.6 | 5.1 | 5.0 | 6.0 | 6.5 | 7.9 | 9.6 | 9.0 | 9.1 | 8.8 | 9.5 | 11.0 | 3.9 |
| Female, % | 8.5 | 4.3 | 4.8 | 4.1 | 6.8 | 8.8 | 8.1 | 10.6 | 10.1 | 10.0 | 9.7 | 10.0 | 4.2 |
| Total, % | 8.6 | 4.8 | 4.9 | 5.2 | 6.6 | 8.3 | 9.0 | 9.7 | 9.5 | 9.3 | 9.6 | 10.6 | 4.0 |

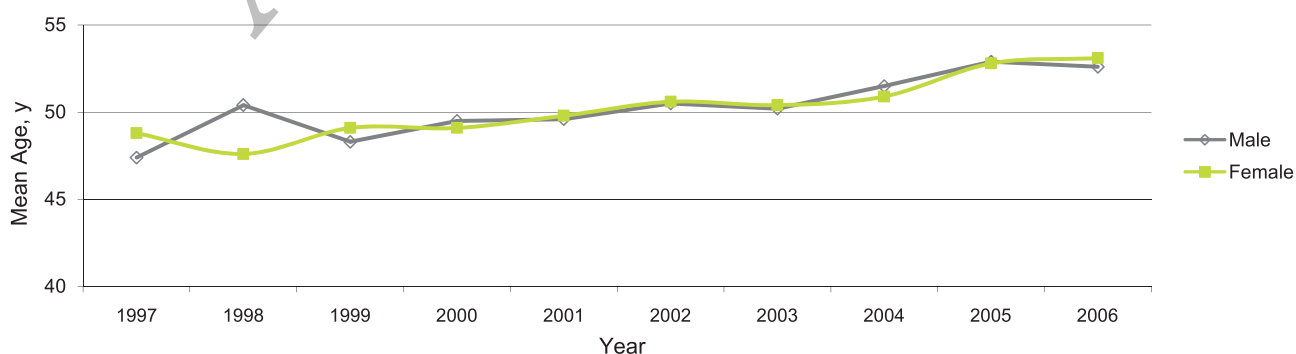


Figure 2. Age and sex distribution trends during a 10-year period in patients with end-stage renal disease in Iran.

DISCUSSION

The age-specific and cause trends in ESRD incidence rates in Iran over the past 10 years has been made accessible in the present study, using the data from the patients registry. The reliability of the present study is high are thanks to the nationwide high-quality RRT registry available in the MOH. By assessing the data, we were able to take into account the aging of incident ESRD population. The prevalence and incidence of ESRD, as measured by the RRT cases, have been increasing in Iran from 137 pmp and 13.82 pmp in 1997 to 238 pmp and 49.9 pmp in 2000 and to 357 pmp and 63.8 pmp in 2006, respectively. Apparently, it was somehow due to the increase in the number of dialysis centers (150 in 1997, 227 in 2000, and 316 in 2006), transplantation centers, nephrologists, and transplantations (living and deceased; 22.8 pmp in 1997 to 26.5 pmp in 2006) in the country. However, the incidence after 2000 shows remarkably faster growth than those in the earlier years,^{5,6} which cannot be explained entirely by the progress of the infrastructure. Meanwhile, by achieving higher standards of hemodialysis; thrice weekly dialysis coverage increased from 50% in 2000 to 60% in 2006.⁶ Bicarbonate-based hemodialysis was started in 2000 and covered 63% of patients on hemodialysis in 2006.⁶ The prevalence of ESRD is also increasing. A similar change as a result of development of the renal care infrastructure has been shown in Romania, following the fall of the communist regimes, with ESRD incidence increased 6 times more than in that 1996, reaching 128 pmp in 2004.⁷ An unexpected finding in our data was a sudden increase of ESRD due to unknown causes in 2000, which we think was the result of unwillingness of physicians for identifying hypertension as the cause of ESRD without biopsy-proven nephrosclerosis. Another finding was the higher prevalence of ESRD in men than women (1.3:1). The results were in concordance with many other studies. The increase in the incidence of diabetes mellitus-associated ESRD in Iran,^{2,8} similar to those in Jordan, Europe, Canada, and the Asia-Pacific region and many others, was in contrast with those in China, Japan, Romania, and Brazil.⁹⁻¹⁷

As a developing country, the achieved standards of RRT in Iran are satisfactory, but they do not seem to be able to catch up with the increasing number

of patients in the coming years. Each country has tackled the problem of increasing number of ESRD in its own way. As glomerulonephritis was the leading cause of ESRD in Japan, national urinalysis screening in adults aged 40 years and over was mandated in the health assessment program in 1983 for early recognition of glomerulonephritis¹⁸; its impact on declining of age-adjusted incidence rate of ESRD attributable to chronic glomerulonephritis started in 1995 to 1996. The decrease in risk may be partly due to improved screening and treatment of glomerulonephritis.¹⁵

There were significant downward trends in the incidence of all-cause or disease-specific ESRD during the years 1998 to 2002 in the European populations and Canadians. Reduction of all-cause ESRD was due to lessening rates of ESRD from each of the primary kidney disease categories that comprise chiefly proteinuric nephropathies, with the important exception of type 2 diabetic nephropathy which had risen substantially.^{11,19} The favorable trend for ESRD in these populations is the encouraging evidence that public health interventions may have curbed the rising rates of ESRD. Diabetic nephropathy, and probably hypertensive nephrosclerosis (as we do not have the biopsies of those who are referred as ESRD due to hypertension), have become the leading causes of ESRD in Iran, as in most countries.⁵⁻⁸

It has been shown in this work that the age-specific incidence rate of all-cause ESRD has increased much more rapidly among the patients older than 60 years compared to other age groups irrespective of sex. These figures are similar to those of the developed world.^{11,12} The rapid increase in the incidence rates in the elderly has been observed in Europe, the United States, Australia, New Zealand, and Japan.^{11,13,15} This highlights that they belong to the high-risk group who should be focused on for chronic kidney disease screening. In contrast, the increase in the ESRD rates slowed down among those younger than 20 years, albeit slowly, but with a significant difference between the period from 1997 to 1998 and the period from 2005 to 2006, possibly due to increased surveillance on kidney disease in childhood and better control strategies.

Considering the number of patients with ESRD in the past 10 years in Iran, it can be inferred that the mean growth rate in this population is 12%. Regarding the foregoing fact, the 2-fold number

of patients with ESRD in the country is predicted in the next 4 years. It means a huge financial burden for the health budget in near future.⁶ An important methodological issue which needs elucidation is that some patients with ESRD might not have undergone RRT, and therefore, we may have underestimated the ESRD incidence. Thus, we should urgently consider preventive strategies, especially with regard to the fact that each month delay of dialysis could save US \$ 1025 in Iran.²⁰

CONCLUSIONS

We strongly recommend considering prevention measures of chronic kidney disease and initial focusing on the strategies and treatment modalities that slow down disease progression, in order to postpone the need for RRT. Otherwise, we should deal with the fact that by 2030, it is estimated that more than 70% of patients with ESRD will be residents of developing countries, whose collective economies will account for less than 15% of the total world economy.¹

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Barsoum RS. Chronic kidney disease in the developing world. *N Engl J Med*. 2006;354:997-9.
2. Batieha A, Abdallah S, Maghaireh M, et al. Epidemiology and cost of haemodialysis in Jordan. *East Mediterr Health J*. 2007;13:654-63.
3. Mahdavi-Mazdeh M, Heidary Rouchi A, Norouzi S, Aghighi M, Rajolani H, Ahrabi S. Renal replacement therapy in Iran. *Urol J*. 2007;4:66-70.
4. Mahdavi-Mazdeh M, Zamyadi M, Nafar M. Assessment of management and treatment responses in haemodialysis patients from Tehran province, Iran. *Nephrol Dial Transplant*. 2008;23:288-93.
5. Perico N, Plata R, Anabaya A, et al. Strategies for national health care systems in emerging countries: the case of screening and prevention of renal disease progression in Bolivia. *Kidney Int Suppl*. 2005S87-94.
6. Aghighi M, Heidary Rouchi A, Zamyadi M, et al. Dialysis in Iran. *Iran J Kidney Dis*. 2008;2:11-5.
7. Mircescu G, Capsa D, Covic M, et al. Nephrology and renal replacement therapy in Romania--transition still continues (Cinderella story revisited). *Nephrol Dial Transplant*. 2004;19:2971-80.
8. Afshar R, Sanavi S, Salimi J. Epidemiology of chronic renal failure in Iran: a four year single- center experience. *Saudi J Kidney Dis Transpl*. 2007;18:191-4.
9. Abdallah S, Ahmad AT, Batieha A, Ajlouni K. Diabetes mellitus: the leading cause of haemodialysis in Jordan. *East Mediterr Health J*. 2007;13:803-9.
10. Van Landeghem MA. [Has the incidence of end-stage renal disease increased in diabetic patients? A center-based longitudinal study over 10 years]. *Med Klin (Munich)*. 2005;100:241-5. German.
11. Stewart JH, McCredie MR, Williams SM, Jager KJ, Trpeski L, McDonald SP. Trends in incidence of treated end-stage renal disease, overall and by primary renal disease, in persons aged 20-64 years in Europe, Canada and the Asia-Pacific region, 1998-2002. *Nephrology (Carlton)*. 2007;12:520-7.
12. Hamer RA, El Nahas AM. The burden of chronic kidney disease. *BMJ*. 2006;332:563-4.
13. Stewart JH, McCredie MR, Williams SM, McDonald SP. Interpreting incidence trends for treated end-stage renal disease: implications for evaluating disease control in Australia. *Nephrology (Carlton)*. 2004;9:238-46.
14. Xie Y, Chen X. Epidemiology, major outcomes, risk factors, prevention and management of chronic kidney disease in China. *Am J Nephrol*. 2008;28:1-7.
15. Wakai K, Nakai S, Kikuchi K, et al. Trends in incidence of end-stage renal disease in Japan, 1983-2000: age-adjusted and age-specific rates by gender and cause. *Nephrol Dial Transplant*. 2004;19:2044-52.
16. Zatz R, Romao JE, Jr. End-stage renal failure and national resources: the Brazilian experience. *Ren Fail*. 2006;28:627-9.
17. Oliveira MB, Romao JE, Jr., Zatz R. End-stage renal disease in Brazil: epidemiology, prevention, and treatment. *Kidney Int Suppl*. 2005S82-6.
18. Imai E, Yamagata K, Iseki K, et al. Kidney disease screening program in Japan: history, outcome, and perspectives. *Clin J Am Soc Nephrol*. 2007;2:1360-6.
19. Foley RN, Collins AJ. End-stage renal disease in the United States: an update from the United States Renal Data System. *J Am Soc Nephrol*. 2007;18:2644-8.
20. Mahdavi-Mazdeh M, Zamani M, Zamyadi M, et al. Hemodialysis cost in Tehran, Iran. *Hemodial Int*. 2008;12:492-8.

Correspondence to:

Mitra Mahdavi-Mazdeh, MD
Emam Hospital, Keshavarz Blvd, Tehran, Iran
Tel: +98 21 6658 1568
Fax: +98 21 6658 1568
E-mail: mmahdavi@sina.tums.ac.ir

Received April 009

Revised June 2009

Accepted June 2009

The abstract of this article had been published in the "Hypertension and the Kidney" ISN-Nexus, 2007.