IJKD KIDNEY DISEASES

The Trend of Mortality Rate and Years of Life Lost Due to Kidney Failure in Fars Province, Iran, During the Years 2004-2019

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Keywords. Kidney failure; Trend; Mortality rate; Years of life lost; Joinpoint regression; Iran

Original Paper

Introduction. Chronic kidney disease is a general term for heterogeneous disorders that affect the structure and function of the kidney. This study was conducted to determine the mortality rate and years of life lost due to kidney failure in southern Iran.
Method. In this retrospective, population-based descriptive trend study, all deaths due to kidney failure in Fars province were extracted from the electronic population-based death registration system (EDRS). The crude mortality rate, age-standardized mortality rate, years of life lost (YLL) and YLL rate data were calculated. The Joinpoint Regression method was used to examine the trend.
Results. During the 16-year study period, 2853 deaths due to kidney failure occurred in Fars province. Of this number, 57.2% (1633 cases) were men. The crude mortality rate had a stable trend in men and an increasing trend in women. However, the age-standardized mortality rate had a stable trend in both sexes. The total years of life lost due to kidney failure were 19366 in men and 15769 in women. According to the Joinpoint regression analysis, the trend of YLL rate due to premature mortality was stable and the annual percent change (APC) were -2.6% (95% CI -5.6 to 0.4, P = .088) and 1.8% (95% CI -1.9 to 5.6, P = .318) for males and females respectively.
Conclusions. The trend of crude mortality rate had a stable trend in men and an increasing trend in women. Also, the trend of YLL was stable for both sexes. The increasing trend in mortality among women may be due to increases in life expectancy and the increasing prevalence of non-communicable diseases such as hypertension and diabetes mellitus.

IJKD 2025;19:322-30
www.ijkd.org

INTRODUCTION

Chronic kidney disease (CKD) refers to a heterogeneous disorders that affect the structure and function of the kidneys.[1] End-stage kidney disease (ESKD) is defined as a glomerular filtration rate (GFR) that is consistently below 15 mL/min per 1.73 m^2.[2] Chronic kidney disease is a public health problem worldwide.[3] As well as chronic kidney disease, acute kidney injury (AKI) is also an important health concern. While it is believed that acute kidney injury is still associated with high mortality, chronic kidney disease poses a major economic burden on health care systems directly or as a risk factor for cardiovascular disease.[4] The progression of chronic kidney disease is usually slow and symptoms become apparent in advanced

stages when the patient progress to ESKD that require renal replacement therapy (RRT).[5]

Each year, more than 115,000 patients with CKD begin maintenance dialysis therapy in the United States.[6] The implications of CKD encompass not just the advancement to renal failure but also consequences arising from decreased kidney function, heightened susceptibility to cardiovascular disease, and an overall increase in mortality risk.[7] According to the Global Burden of Diseases study, chronic kidney disease has increased from the 36th leading cause of death in 1990 to the 19th leading cause of death in 2013.[8]

In a study conducted in the Fars province of Iran, hypertension and diabetes mellitus were the most common causes of chronic kidney disease.[9] The Global Burden of Disease Study showed that chronic kidney disease accounts for only 20% of the disability-adjusted life years (DALY) from years lived with disability (YLD) and 80% from years of life lost (YLL). Worldwide in 1990, 72.5 YLD per 100,000 and 329.5 YLL per 100,000 were caused by chronic kidney disease, while in 2019 they were 113.0 and 423.8, respectively.[10]

The years of life lost (YLL) is an important criterion for ranking the health status of society and observing their challenges. According to the report of the World Health Organization, the value of one year of life is three times more than the gross domestic product (GDP) per capita of any country.[11] The prevalence of chronic kidney disease in the Iranian population is high.[12] Since no study has been conducted to determine the years of life lost due to kidney failure in Fars province, this study was designed to determine the mortality rate and years of life lost due to kidney failure in southern Iran.

MATERIALS AND METHODS

In this retrospective, population-based descriptive trend study, data of Fars province were collected from 2004 to 2019. We obtained all deaths attributable to kidney failure (both chronic and acute) through the population-based Electronic Death Registration System (EDRS) categorized by age, sex, and year of death, in accordance with ICD-10. During the data collection period, the Iranian national death registry employed ICD-10 coding, as ICD-11 had not yet been implemented. The codes used in this study were N17 (Acute renal failure) and N18 (Chronic renal failure). This study aimed to investigate the mortality rate and years of life lost attributable to ESKD. Within the population-based electronic death registration system, all available sources including hospitals, health care centers, civil registries, and forensic organizations were used to detect, record and collect information related to death; repeated deaths were excluded from the study.[13]

The total estimated population of Fars province was estimated using the basic data of health centers and the population and housing census from 1996 to 2016, taking into account the annual population growth. For direct standardization, the 2013 standard population for low- and middle-income countries was used. This standard population gives more weight to younger people than the standard population of the World Health Organization, making it more suitable for these settings.[14]

Statistical analysis

First, crude and age-standardized mortality rates (ASR) of kidney failure were calculated during the study years according to gender and year of death.

Then, YLL were calculated using the standard life table to determine the life expectancy for different age and sex groups, as well as the number of deaths due to kidney failure, in each age and sex group, based on the following formula.[15]

$$YLL = N\,C\,e^{(ra)} / (\beta+r)^2\,[e^{-(\beta+r)(L+a)}\,[-(\beta+r)(L+a)-1] - e^{-(\beta+r)a}\,[-(\beta+r)a-1]]$$

Where

N: Number of deaths of a particular sex and age.

L: Standardized life expectancy of the deceased at the same age and sex.

r: Discounting Rate (0.03).

β: The contractual rate in calculating the age (0.04).

C: An adjusted constant (0.1658).

a: Age at death.

e: Mathematical Euler's constant (approximately 2.71).

Initially, the years of life lost were calculated for 18 age groups: 0-4, 5-9, 10-14, etc. up to 85 years old. Subsequently, the results were aggregated into broader age groups (0-4, 5-14, 15-29, 30-44, 45-59, 60-69, 70-79 and over 80 years) for presentation in a figure.

The analysis of the years of life lost due to

premature death from kidney failure was performed using the World Health Organization's 2015 YLL template in Microsoft Excel version 2016 spreadsheet software.

To examine the trend of crude and standardized mortality rates and YLL rates over time, joinpoint regression based on the log-linear model was used. Joinpoint regression analysis describes changing trends over successive segments of time and the amount of increase or decrease within each segment. The resulting line segment between joinpoints is described by the annual percent change (APC), which is based on the slope of the line segment and the average annual percent change (AAPC). The analysis was carried out using the Joinpoint Regression Program, version 4.9.1.0.

The study protocol was reviewed and approved by the Ethics Committee of Shiraz University of Medical Sciences. All aspects of the study were conducted according to the university's code of ethics.

RESULTS

During the 16-year study period, 2853 deaths due to kidney failure occurred in Fars province. Of these, 57.2% (1633 cases) were men and 33.0% (941 cases) were in the age group above 80 years.

As seen in Table 1, the crude mortality rate due to kidney failure had stable trend in males (P = .530) and an increasing trend in females (P = .048). Similarly, the standardized mortality rate had a stable trend in both males and females, (P = .936) and (P = .730), respectively.

The highest and lowest number of deaths in both sexes were in the age groups above 80 years and 5-14 years, respectively (Figure 1).

Temporal trends of kidney failure mortality by age groups

In the 0–44 age group, the kidney failure mortality rate showed stable trends for both men (AAPC = –5.6%, P = .056) and women (AAPC = –0.9%, P = .582).

In the 45–59 age group, there was a decreasing trend in men (AAPC = -8.2%, P = .002) and a stable trend in women (AAPC = -4.3%, P = .216).

In the 60–74 age group, there were stable trends in both men (AAPC = 2.1%, P = .737) and women (AAPC = 1.1%, P = .661). Similarly, in the ≥75 age group, stable mortality rate trends were found in both men (AAPC = 4.0%, P = .158) and women (AAPC = 2.1%, P = .183).

The total years of life lost (YLL) due to kidney failure during the 16-year study period were 19366 (0.6 per 1000 people) in men, 15769 (0.5 per 1000 people) in women, and 35135 (0.6 per 1000

Table 1. Crude and standardized mortality rate (per 100,000 population) and years of life lost due to kidney failure by sex and year in Fars province during 2004-2019.

Year	No. death		Crude mortality rate		ASR (95%CI)		YLL				% (Total YLL)
							No.		(per 1000)		
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Total
2004	92	53	4.9	3.0	6.9 (5.9-7.9)	3.8 (3.0-4.6)	1374	898	0.7	0.5	0.9
2005	73	45	3.9	2.5	4.8 (3.8-5.8)	3.4 (2.7-4.1)	1025	619	0.6	0.3	0.6
2006	103	79	5.6	4.4	7.1 (6.0-8.2)	5.7 (4.7-6.7)	1544	1170	0.8	0.6	1.0
2007	96	65	5.1	3.6	6.0 (5.0-7.0)	4.0 (3.1-4.9)	1216	790	0.7	0.4	0.7
2008	117	59	6.2	3.2	6.9 (5.8-8.0)	3.8 (3.0-4.6)	1478	773	0.8	0.4	0.8
2009	97	65	5.1	3.5	5.2 (4.2-6.2)	4.1 (3.2-4.9)	1206	872	0.6	0.5	0.8
2010	104	60	5.4	3.2	5.3 (4.3-6.3)	3.3 (2.5-4.1)	1154	740	0.6	0.4	0.7
2011	131	95	6.7	4.9	7.2 (6.1-8.3)	5.4 (4.4-6.4)	1640	1347	0.8	0.7	1.2
2012	119	108	6.0	5.6	6.0 (4.9-7.1)	6.1 (5.1-7.1)	1530	1485	0.8	0.8	1.1
2013	71	54	3.6	2.7	3.4 (2.5-4.2)	2.8 (2.1-3.5)	662	677	0.3	0.3	0.5
2014	72	50	3.6	2.5	3.2 (2.4-4.0)	2.3 (1.6-3.0)	772	597	0.4	0.3	0.5
2015	89	73	4.3	3.6	4.3 (3.4-5.2)	3.7 (2.9-4.5)	1064	1076	0.5	0.5	0.9
2016	92	71	4.4	3.5	4.0 (3.1-4.9)	3.2 (2.4-4.0)	916	739	0.4	0.4	0.7
2017	128	113	6.2	5.6	5.9 (4.8-7.0)	5.2 (4.2-6.2)	1303	1314	0.6	0.6	1.0
2018	122	117	5.8	5.7	5.4 (4.4-6.4)	5.3 (4.3-6.3)	1167	1355	0.6	0.7	1.0
2019	127	113	6.0	5.5	6.0 (4.9-7.1)	5.1 (4.1-6.1)	1315	1317	0.6	0.6	1.0
Total	1633	1220	5.2	4.0	5.4 (5.2-5.6)	4.2 (4.0-4.4)	19366	15769	0.6	0.5	0.8
P value	-	-	0.530	0.048	0.936	0.730	-	-	0.088	0.546	0.587

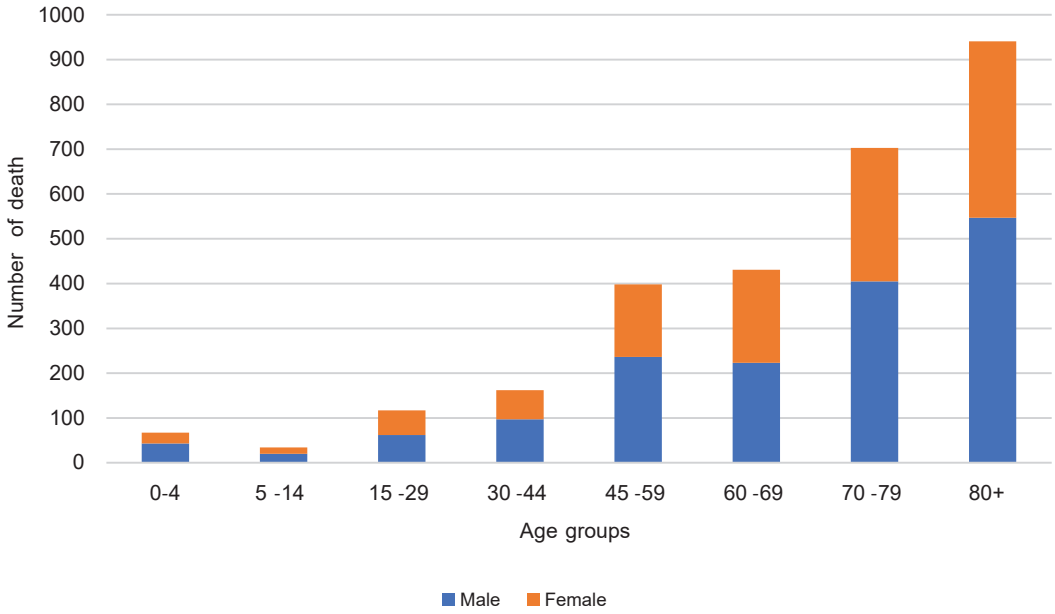


Figure 1. Number of deaths due to kidney failure by gender and age groups.

people) in both sexes combined (male to female ratio: 1.2; Table 1).

The average years of life lost due to kidney failure was 11.8 years in men and 12.9 years in women. The 45-59 age group had the highest YLL whereas the 5-14 age group presented the lowest YLL in both genders respectively. (Figure 2).

As described in Table 1, the trend of years of life lost due to kidney failure remained stable compared to years of life lost due to all-cause mortality (P = .730).

According to the joinpoint regression analysis, the trend of YLL rate due to premature mortality was stable for males, females and both sexes: the annual percent change (APC) was -2.6% (95% CI -5.6 to 0.4, P = .088), 1.8% (95% CI -1.9 to 5.6, P = .318) and -1.0% (95% CI -4.3 to 2.5, P = .546), respectively. The model did not show any join

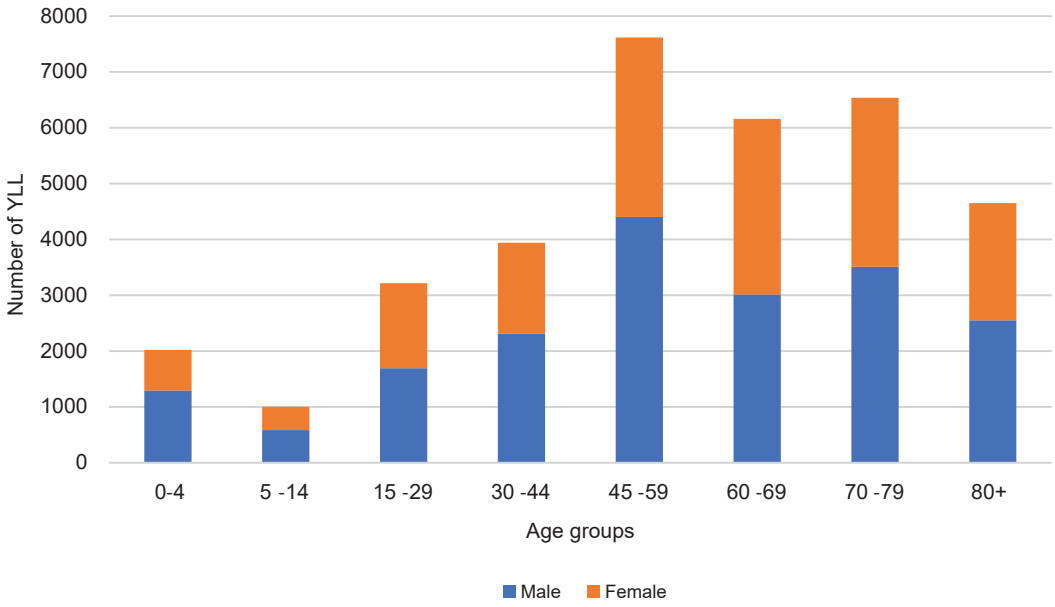
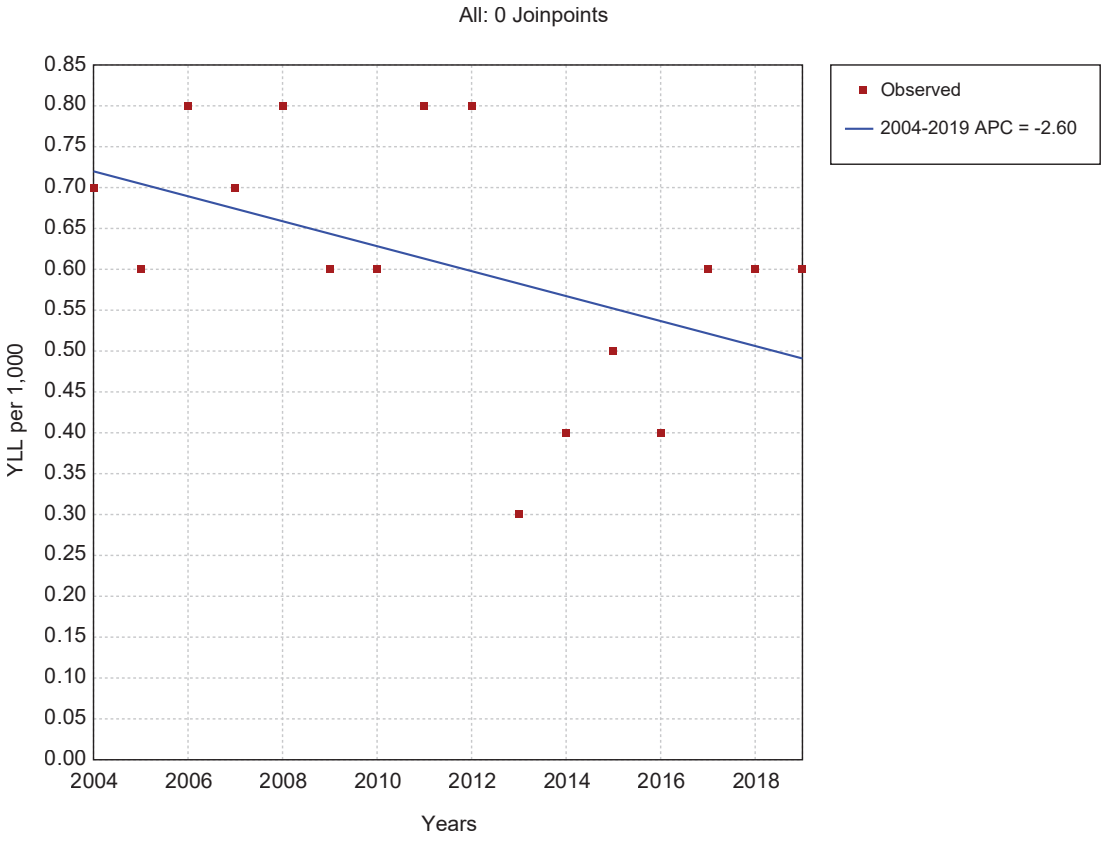


Figure 2. Years of life lost due to kidney failure by gender and age groups.



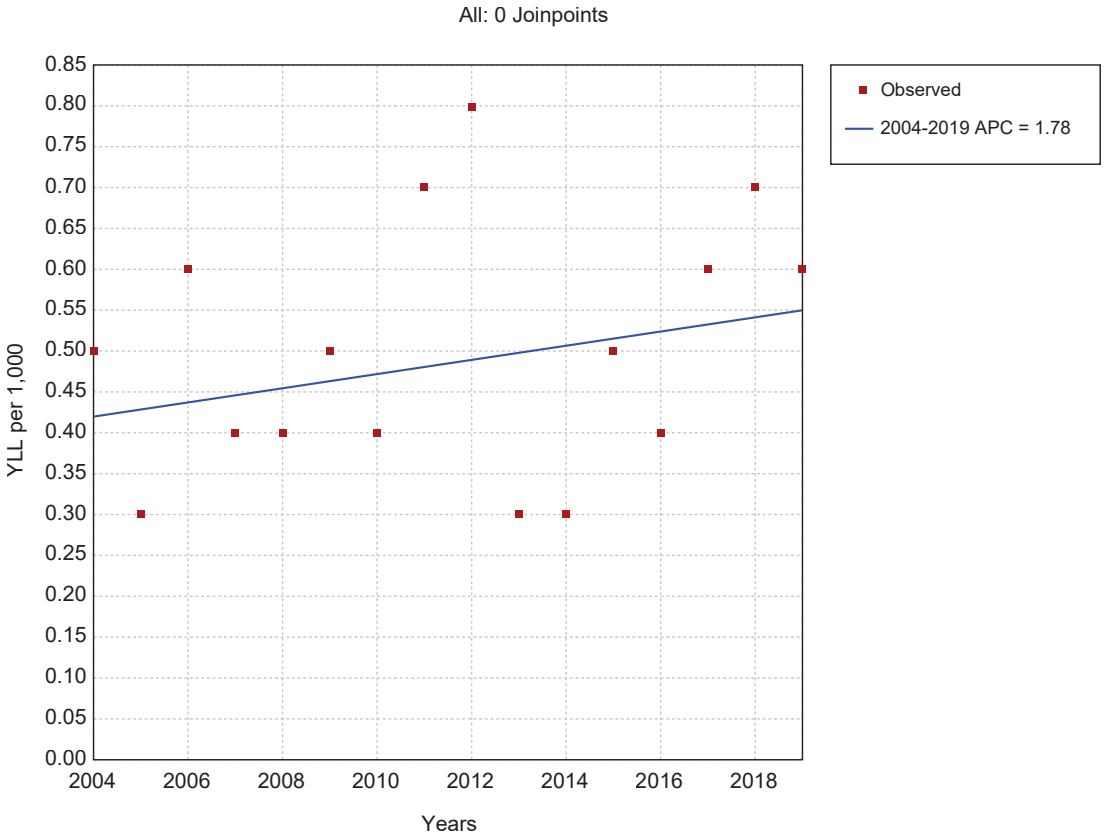
* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level
Final Selected Model: 0 Joinpoints.

Figure 3. The trend of the years of life lost due to kidney failure in men during the years 2004-2019.

point; hence, the AAPC (Average Annual Percent Change) is the same as APC. (Figures 3, 4).

DISCUSSION

In this study, we investigated the mortality rate and YLL due to kidney failure in Fars province (southern Iran) and its trend over the course of 16 years. Our main findings revealed that the trends of the age-standardized mortality rate and YLL rate due to kidney failure were almost unchanged in men and women. Individuals aged over 80 years exhibited the highest mortality rates in both sexes, whilst the 5-14 age group demonstrated the lowest mortality rates in comparison. In contrast, the 45-59 age group exhibited the highest YLL for both sexes, and the 5-14 age group demonstrated the lowest recorded YLL. Chronic kidney disease (CKD) is a potentially life-threatening condition that affects millions of people and creates a heavy burden worldwide.[16] One of the key measures of the impact of kidney failure is the concept of "years of life lost" or YLL. However, the crude mortality rates showed a stable trend in men and an increasing trend in women during this period. Other studies have stated that the prevalence and mortality rate of chronic kidney disease has increased significantly in recent decades. The age-standardized mortality rate of CKD worldwide has increased by 13.33% between 1990 and 2019.[16] Wen *et al.* compared the burden of CKD in high-income countries between 1990 and 2019 and showed that the age-standardized mortality rate and disability-adjusted life years (DALY) have decreased in China, Japan, England, except for the United States that these rates have increased. However, the incidence of CKD and its morbidity and mortality has increased significantly in all four countries.[17] An Australian study showed that the age-standardized mortality has remained relatively constant between 2000 and 2020 in both sexes.[18] In most studies, it has been shown that the crude mortality rate has increased significantly, while the



* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level
Final Selected Model: 0 Joinpoints.

Figure 4. The trend of the years of life lost due to kidney failure in women during the years 2004-2019.

standardized mortality rate has either decreased or remained constant, which is in line with the results of our study. This difference between the crude and standardized rate indicates that the reason for the increase in the crude death rate and mortality is largely due to the aging of the population, increased life expectancy and lifestyle changes, and escalation of the risk factors such as diabetes mellitus and hypertension, which is mentioned in other studies.[17,19-21] In our study, although the age-standardized mortality rate in men remained almost constant during the study period, it increased in women. However, the overall rate was still higher in men than in women. This increase among women may be due to the relatively higher and rising prevalence of risk factors such as diabetes mellitus and hypertension in Iranian women compared to Iranian men.[22,23]

Recent clinical and epidemiological studies in Iran have provided more insight into the underlying causes and risk factor profiles of CKD, which can help interpret the findings of our study. Several cohort studies have confirmed that diabetes mellitus, hypertension, obesity, and elevated triglycerides are among the most significant modifiable risk factors contributing to CKD incidence in the Iranian population. For instance, data from the Shahedieh cohort in Yazd province showed that individuals with obesity (OR 1.40), diabetes (OR 1.38), and hypertension (OR 1.18) were significantly more likely to develop CKD compared to those without these conditions.[24] Moreover, findings from the Tehran Lipid and Glucose Study (TLGS) indicated that changes in metabolic syndrome status over a three-year period were associated with a hazard ratio of 1.22 to 1.34 for incident CKD, suggesting that the dynamic control of risk factors can reduce the disease burden.[25]

In line with other studies, the mortality rate due to CKD is higher in men than in women,[17] however, this rate in our study is much lower in both sexes than in studies conducted in the

Netherlands,[10] China,[19] Japan, England and the United States.[17] According to other studies, YLL due to CKD is high in European countries, such as Greece 538, Germany 467, Australia 429, Netherlands 185, and the European Union 284 per 100,000 population, which is significantly higher compared to the findings of our study that YLL is 60 per 100,000 population.[10,26] The trend of YLL has been increasing in both sexes from 1990 to 2019 regardless of the income level,[27-30] however, in our study, YLL is generally more prevalent in men than women, and the trend of YLL was stable in both men and women. Many studies have depicted the gender differences in terms of YLL align with or contradict to the findings of our study.[27,31] The reasons for these discrepancies are unclear and probably complicated, but the reasons for the increasing trend of YLL among the women in our study can be explained as follows. The prevalence of key CKD risk factors such as obesity, high blood pressure, and diabetes, has been increasing in women in recent years,[32-34] and in addition, women may be more involved in behaviors such as smoking cigarettes and tobacco, which can increase the risk of CKD.[35-39]

Strengths and limitations

One of the limitations of the study is that acute and chronic kidney failure were merged together due to the limitations of ICD-10 codes; this may cause fluctuations in the results. Besides, our study was conducted in one province; however, this study can be generalized to other regions of Iran due to the relatively large sample size.

CONCLUSION

The trend of crude mortality due to kidney failure in men has been rising, although this trend lacked statistical significance. In women, however, this trend showed a significant increase. Furthermore, the trend of YLL remained stable in both men and women. This study showed that the problem of premature mortality due to kidney diseases affects men more than women. This increasing trend in women may be due to the increased life expectancy, higher prevalence of non-communicable diseases such as hypertension and diabetes mellitus, or improved patient survival due to better care. Therefore, policymakers should be concerned and well-informed about this increase. Further studies are needed to investigate the reasons behind these increasing and stable trends.

ETHICAL APPROVAL

The study protocol was reviewed and confirmed by the Ethics Committee of Shiraz University of Medical Sciences (SUMS) (code: IR.SUMS.REC.1399.772).

CONFLICT OF INETEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

AH was responsible for the field working including data collection and management and wrote the manuscript. BN was collected data and wrote the manuscript. HJ analyzed data and wrote the manuscript. MA collected data and edited the final version of the manuscript SHI and DSP conception and design of the study and wrote the manuscript. All authors have approved the final version of manuscript.

AVAILABILITY OF DATA AND MATERIALS

The data are available from the corresponding author upon reasonable request.

FUNDINGS

None.

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Received December 2023
Revised April 2025
Accepted October 2025