Epidemiology of end-stage renal disease in the countries of the Gulf Cooperation Council: a systematic review

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DECLARATIONS

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Summary

Objectives To describe the epidemiology of end stage renal disease (ESRD).

Design Mixed-methods systematic review.

Setting The countries of the Gulf Cooperation Council (GCC) which consist of Saudi Arabia, the United Arab Emirates, Kuwait, Qatar, Bahrain, and Oman.

Participants Defined to have ESRD or patients on regular dialysis for a minimum dialysis period of at least three months. Since many outcomes were reviewed, studies that estimated the incidence and prevalence of ESRD as outcomes should not have defined the study population as ESRD population or patients on regular dialysis. Studies where the study population mainly comprised children or pregnant woman were excluded.

Main outcome measures The trends of the incidence, prevalence, and mortality rate of ESRD; also, causes of mortality, primary causes and co-morbid conditions associated with ESRD.

Results 44 studies included in this review show that the incidence of ESRD has increased while the prevalence and mortality rate of ESRD in the GCC has not been reported sufficiently. The leading primary causes of ESRD recorded in the countries of the GCC is diabetes with the most prevalent co-morbid conditions being Hypertension and Hepatitis C Virus infection; the most common cause of death was cardiovascular disease and sepsis.

Conclusions This review highlights that the lack of national renal registries data is a critical issue in the countries of the GCC. The available data also do not provide an accurate and updated estimate for relevant

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outcomes. Additionally, considering the increasing burden of chronic kidney disease (CKD), these results stressed the needs and the importance of preventative strategies for leading causes of ESRD. Furthermore, more studies are needed to describe the epidemiology of ESRD and for assessing the overall quality of renal care.

Introduction

End-stage renal disease (ESRD) is defined as irreversible decline in kidney function, when renal replacement therapy (RRT) is needed for survival. There are two main types of RRT: dialysis and kidney transplantation.[1] Kidney transplantation is preferred for patients with ESRD since it offers a longer life span, superior quality of life, and is more cost effective than long-term dialysis.[2] ESRD has become a public health concern worldwide, with recent reports showing that the total number of ESRD patients has been growing dramatically.[3–8] The rising prevalence is due largely to two main factors; the ageing of the population and the global epidemic of diabetes.[3]

The countries of the Gulf Cooperation Council (GCC), which consist of Saudi Arabia, the United Arab Emirates, Kuwait, Qatar, Bahrain, and Oman, share a similar background of culture and ethnicity, while their socio-demographic distributions and socioeconomic development are also similar.[4] Although the countries of the GCC have experienced noticeable advances in delivering healthcare, the burden of non-communicable diseases is increasing rapidly.[5] Many reports have shown evidence of increasing prevalence of the most common causes of ESRD in the GCC: the prevalence of obesity in these countries, which is associated with multi-chronic diseases, exceeds that in the developed countries because of their rapid economic growth and associated changes in lifestyle.[6–8] Furthermore, the International Diabetes Federation reports that five of the countries of the GCC ranked globally among the top ten countries in the world for diabetes prevalence.[9]

The growing incidence of ESRD is increasing the use of RRT, as well as generating greater morbidity, and more hospitalizations. These in turn increase healthcare expenditures, placing a heavy financial burden on healthcare providers and general populations to meet the growing needs of patients with ESRD.[10,11] However, ESRD has a significant effect on public health in the countries of the GCC, as the policy of these countries provides free health services including RRT to the population based on clinical need without any restrictions in terms of age, gender, or social status. Because the majority of RRT facilities are provided by the governmental sector, any increase in its use would be associated with a significant increase of healthcare expenditures.

ESRD also has a significant effect on quality of life and life expectancy.[12] Most patients receive haemodialysis treatment for ESRD by being connected three times per week to a dialysis machine for several hours at a time. People with ESRD are more likely than those without the illness to develop cardiovascular disease, the most common cause of death in those with ESRD.[13]

Scarce data is available on the epidemiology of ESRD in the countries of the GCC. In the absence of national renal registries system in these countries, data that do exist are unsatisfactory and insufficient: most data are either recorded by referring centres rather than community hospitals such as Saudi Centre for Organ Transplantation (SCOT) data; or based on small studies. However, analyses of the epidemiology of ESRD itself in this region are also inconsistent. For example, the prevalence of ESRD decreased between 1986 and 2005, a period when risk factors for the disease became more common; this might be due to underreporting the cases of ESRD[14,15] or might be influenced by mortality and renal transplant rate. Other articles report inconsistent results of primary causes of ESRD.[11,16] These conflicting analyses of the epidemiology of ESRD mean that synthesizing and assessing the evidence available would be valuable.

This review was conducted to synthesize the results of all relevant studies to describe the epidemiology of ESRD in the countries of the GCC based on: incidence, prevalence, patient characteristics (age, sex, RRT), primary causes, co-morbidities associated with ESRD, mortality

rate and causes of death in the ESRD population. This was done by indentifying and reviewing the published epidemiological studies of ESRD in the countries of the GCC.

Methods

Systematic review

A systematic review was conducted by searching Medline and EMBASE databases, to identify all relevant papers published from 1950 until May 2010; using the following keywords in the searching strategy:

> *End stage, terminal, chronic, renal, kidney, Arab, Middle East, Arabian Gulf, Saudi Arabia, Kuwait, and United Arab Emirates, Oman, Qatar, and Bahrain.*

Additionally, the reference lists of all identified papers were reviewed to identify other papers, which were not identified in the database search.

All the titles and abstracts of references were reviewed independently by two reviewers to identify relevant papers. Then, the full texts of the papers were reviewed to identify epidemiological studies that fulfilled the following criteria: any observational epidemiological study including cohort studies, case control studies, cross-sectional studies, and ecological studies; reporting ESRD incidence, prevalence, primary causes, co-morbidities conditions, mortality rate/causes were included in this review. In addition, all the studies have been defined by the study population to have ESRD or involve patients on regular dialysis for a minimum dialysis period of at least three months in any of the countries of the GCC. Since many outcomes were reviewed in this systematic review, studies that estimated the incidence and prevalence of ESRD as outcomes should not have defined the study population as ESRD population or patients on regular dialysis. Studies where the study population mainly comprised children, or pregnant woman, or patients on regular dialysis without mentioning the dialysis period or a period less than three months were excluded. In addition, the studies that do not report any statistical information about any relevant outcomes were excluded.

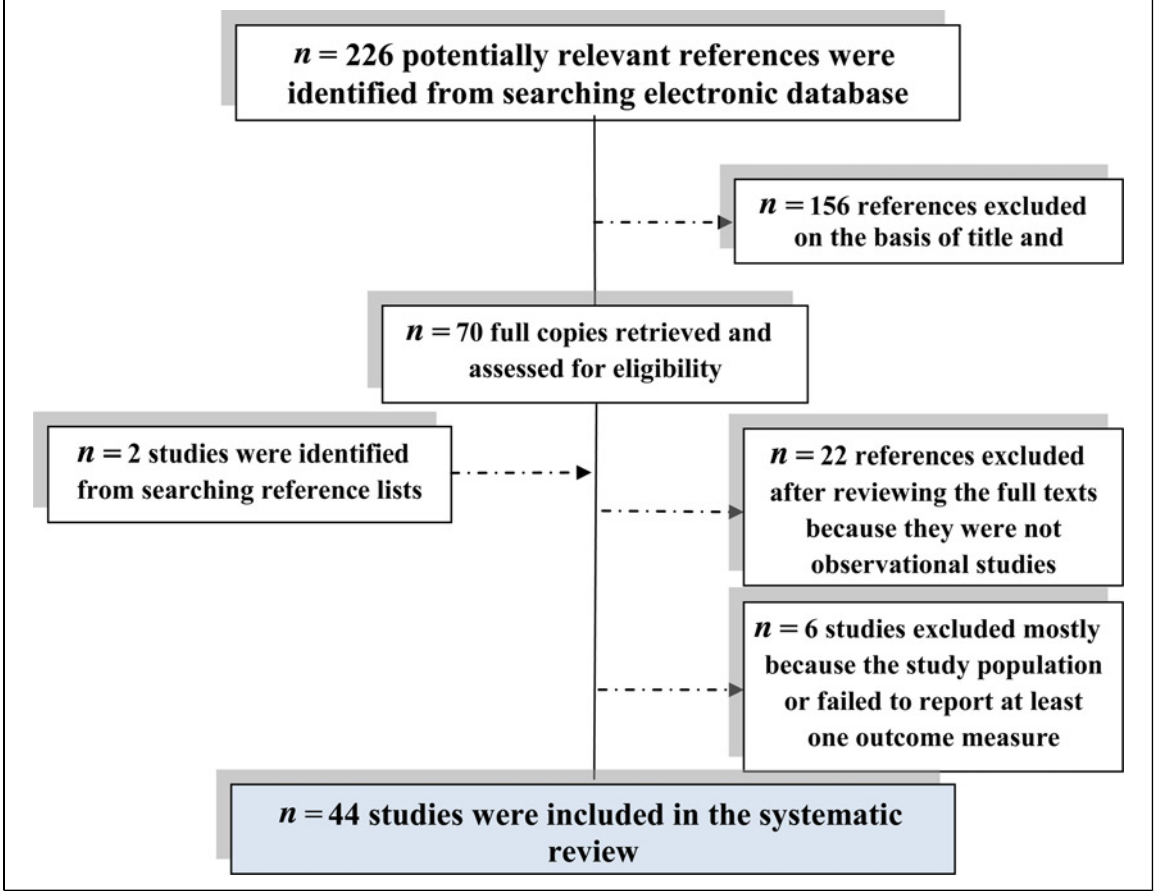
Studies that met the inclusion criteria for the review had data extracted. Data relating to study design, setting, definition of outcomes measure, inclusion and exclusion criteria of study population, methodological quality using the Newcastle Ottawa Scale (NOS)[17] and outcomes were then independently extracted by two reviewers using standardized data extraction form. In methodological quality assessment NOS, the included studies were classified after aggregating the score as follows: scores of seven or higher were chosen to indicate higher methodological quality, a score less than seven indicates a lower methodological quality.

Some outcomes such as primary causes and co-morbidities were classified as follows: primary causes of ESRD were classified as in the ICD9-CM code, which was updated in 2008 because there were no studies in this review used standardized methods to classify the primary causes. Co-morbidities associated with ESRD were classified into three groups: chronic diseases, infectious diseases, and other co-morbidities.

Data analysis

The extracted data for patients' characteristics, prevalence, incidence, and mortality rate of ESRD were analyzed descriptively. The data related to primary causes, co-morbidities, and causes of death were entered to STATA version 10 for statistical analysis. These data were then used to conduct meta-analysis to summarize the prevalence of each outcome where possible. The degree of heterogeneity was assessed between the studies statistically using meta-analysis to obtain an I-square value.[18] This review combined the results from observational studies, therefore it would be expected that the value of I-square would be high due to sampling, methodological and statistical variation of the studies. To account for the anticipated heterogeneity, the random effect method was used to combine the measure of effect (DerSimonian and Laird model). Subgroup analysis was performed when it was needed to investigate the reasons for heterogeneity between the studies; it was used to assess the differences between locations and time. Furthermore, the measures of uncertainty (95% confidence intervals (CIs) were calculated where

Figure 1
Flow chart shows a summary of the systematic literature review



meta-analysis was not appropriate to conduct for any outcome especially for those that reported in less than three studies.

Results

The search identified 226 articles published from 1950 to May 2010. After reviewing the titles and abstracts, 70 were obtained for full text review and 156 excluded. Twenty-two studies were excluded after reviewing the full text, and two studies were included after reviewing the reference lists of each paper. Fifty studies were eligible for data extraction; six studies were excluded due to the nature of the study population or because they failed to report any outcome measures of interest. Mitwalli (1991)[19] and Al-Shohaib (1999)[20] were excluded because, although the study population was defined as dialysis patients, no further background was provided, such as the dialysis period, and it might have included patients with acute renal failure. Al-Mohaya (1990)[21] Yahya (1998)[22] Rafi (2007)[28] and Al-Jahdali (2009)[29] were excluded because no relevant statistical outcomes were reported (Table 1). After the search inclusions and exclusions, 44 epidemiological studies were eligible for the systematic review. (Figure 1)

Characteristics of included studies

There were 40 studies conducted in Saudi Arabia in different regions. One study was conducted in the United Arab Emirates/Abu-Dhabi,[23] one was conducted in Kuwait,[24] one was conducted in

Table 1
Summary of excluded studies

Ref	*Author*	*Year*	*Title*	*Study design*	*Location*	*Study design*	*Population size*	*Age range*	*Male %*	*RRT*	*Quality*
21	Al-Mohaya	1990	Arteriovenous fistula for haemodialysis a report of 112 consecutive cases	Cross-sectional	KSA/East-Al-Khobar	Cross-sectional	112	13–75	59.8	HD/RT	2
19	Mitwalli	1991	Tuberculosis in patients on maintenance dialysis	Cross-sectional	KSA/Centre-Riyadh	Cross-sectional	25	34–40	26	–	3
22	Yahya	1998	Analysis of 490 kidney biopsies data from the United Arab emirates renal disease registry	Cross-sectional	UAE/Abodabhi	Cross-sectional	490	14–66	NR	–	3
20	Al-Shohaib	1999	Tuberculosis in active dialysis patients in Jeddah	Cross-sectional	KSA/West-Jeddah	Cross-sectional	210	NR	NR	–	2
56	Rafi	2007	Monitoring iron status in end-stage renal disease patients on haemodialysis	Cross-sectional	KSA/East-Damam	Cross-sectional	24	29–65	79	–	1
57	Al-Jahdali	2009	Advanced care planning preferences among dialysis patients and factors influencing their decisions	Cross-sectional	KSA/Centre-Riyadh	Cross-sectional	100	36–66	53	–	2

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Table 2
Summary of included studies

Ref.	*Author*	*Year*	*Title*	*Study design*	*Location*	*Quality*	*Mean of age*	*Age range*	*Male %*	*RRT*			*ESRD patients*
										HD%	*PD%*	*RT%*	
41	Al-Nasser	1992	Seropositivity to hepatitis C virus in Saudi haemodialysis patient	Case control	KSA/South-Baha	5	46	30–68	53.81	100	–	–	66
39	Mitwalli	1992	Hepatitis C in chronic renal failure patients	Case-control	KSA/Centre-Riyadh	2	NR	NR	NR	86.6	13.3	–	30
58	Al-Ghamdi	1998	Whole blood total, reduced and oxidized ascorbic acid levels in Saudi patients with chronic renal failure: influence of gender and chronic haemodialysis	Case-control	KSA/Centre-Riyadh	4	33	23–43	50.98	100	–	–	55
25	Al-Haddad	2003	Depression among end stage renal disease patients	Case control	Bahrain	4	52	NR	46.7	100	–	–	45
55	Al-Mueilo	2004	Gastro-duodenal lesions and Helicobacter pylori infection in haemodialysis patients	Case control	KSA/East-Khobar	3	NR	16–85	59	100	–	–	54
36	Al-Ali	2008	Increased prevalence of glycoprotein IIB/IIIa Leu 33 pro polymorphizm in end stage renal disease patients on haemodialysis	Case-control	KSA/East-Dammam	7	50	38–65	68	100	–	–	42

47	Hussein	1990	Tuberculosis in patients undergoing maintenance dialysis	Cohort	KSA/West-Taief	4	42	20–60	26	62.4	13.17	–	205
23	Shakuntala	1992	End-stage renal disease in native population of the United Arab Emirates	Cohort	UAE/ Abudhabi	4	45	11–75	NR	52.1	–	47.9	96
24	El-Reshaid	1994	End-stage renal disease and renal replacement therapy in Kuwait-epidemiological profile over the past $4^{1/2}$ years	Cohort	Kuwait	7	NR	NR	63.7	75.1	21.2	3.7	647
59	Mitwalli	1995	The incidence of end-stage renal disease in two regions of kingdom of Saudi Arabia	Cohort	KSA/Gaizan, Madinah	7	NR	11–75	61	–	–	–	Madinah = 108, Gaizan = 187, Total = 295
26	Al-Homrany	1998	Incidence of treated end-stage renal disease in Asir region, southern Saudi Arabia	Cohort	KSA/South-Asir	8	47.89	9–99	56.1	–	–	–	114
30	Al-Muhanna	1999	Disease profile complications and outcome in patient on maintenance haemodialysis at King Faisal University hospital, Saudi Arabia	Cohort	KSA/East-Khobar	6	45.5	34–57	65.6	100	–	–	233
27	Suberamanian	2001	Haemodialysis utilization in a single in-centre dialysis unit, in the kingdom of Saudi Arabia	Cohort	KSA/South-Gizan	4	40.7	10–93	46.6	86.5	–	13.5	393

(Continued)

Table 2
Continued

Ref.	Author	Year	Title	Study design	Location	Quality	Mean of age	Age range	Male %	RRT			ESRD patients
										HD%	PD%	RT%	
50	Youmbissi	2001	CAPD in Dammam central Hospital, Saudi Arabia: a Five year experience	Cohort	KSA/East-Dammam	3	41.3	10–85	32.25	–	100	–	31
28	Al-Wakeel	2002	Morbidity and mortality in ESRD patients on dialysis	Cohort	KSA/Centre-Riyadh	4	53.8	17–92	64.5	59.1	29.1	11.8	110
60	Shaheen	2002	Pre-end stage chronic renal failure: the Jeddah kidney centre experience	Cohort	KSA/West-Jeddah	6	49.5	11–90	58.6	–	–	–	99
32	Saxena	2003	The susceptibility of patients with type-2 diabetes to hepatitis C virus infection during long-term haemodialysis	Cohort	KSA/East-Hafouf	7	52.8	14–84	50.51	100	–	–	196
49	Saxena	2003	The prevalence of Nasal carriage of staphylococcus aureus and associated vascular access-related septicaemia among patients on haemodialysis in Al-Hasa region of Saudi Arabia	Cohort	KSA/East-Hafouf	3	47.5	15–84	45.7	100	–	–	208
29	Al-Khunaizi	2003	End stage renal disease experience in a general hospital in	Cohort	KSA/East-Dhahran	4	60	NR	50	97.8	2.2	–	37

			eastern Saudi Arabia										
61	Mohamed	2004	Incidence and aetiology of end-stage renal disease in Madinah Munawarah Area: Any changing trends?	Cohort	KSA/West-Madinah	5	NR	>13	61.6	–	–	–	106
62	Saxena	2004	The impact of nurse understaffing on the transmission of hepatitis C virus in a hospital-based haemodialysis unit	Cohort	KSA/East-Hafouf	7	47	15–84	54	100	–	–	198
44	Saxena	2004	The vulnerability of middle-aged and elderly patients to hepatitis C virus infection in a high-prevalence hospital-based haemodialysis	Cohort	KSA/East-Hafouf	6	47	15–84	54	100	–	–	198
48	Saxena	2004	Advancing age and the risk of nasal carriage of staphylococcus aureus among patients on long-term hospital-based haemodialysis	Cohort	KSA/East-Hafouf	6	NR	15–84	46.8	100	–	–	205
63	Mohamed	2005	Morbidity and mortality in ESRD patients on regular haemodialysis: a single centre experience	Cohort	KSA/West-Madinah	4	51	13–85	58.5	100	–	–	395

(Continued)

Table 2
Continued

Ref.	Author	Year	Title	Study design	Location	Quality	Mean of age	Age range	Male %	RRT			ESRD patients
										HD%	PD%	RT%	
64	Al-Khunaizi	2007	Patterns of renal pathology among renal biopsy specimens in eastern Saudi Arabia	Cohort	KSA/East-Dhahran	6	41	23–59	55	–	–	–	95
65	Hussein	1990	Chronic intermittent peritoneal dialysis using automatic cycler machine	Cross-sectional	KSA/West-Taief	1	NR	6–74	42	–	100	–	28
38	Fakunle	1991	Prevalence of antibodies to hepatitis C virus in haemodialysis patients in Riyadh	Cross-sectional	KSA/Centre-Riyadh	3	40.4	15–75	63.2	100	–	–	190
14	Ibrahim	1992	End-stage renal disease (ESRD) in Saudi Arabia	Cross-sectional	KSA	2	NR	NR	50.7	98	2	–	822
34	Hussein	1994	Observations in Saudi Arabian dialysis population over a 13-year period	Cross-sectional	KSA/West-Taief	4	43	6–89	53.84	63.8	1.2	35	325
37	Huraib	1995	High prevalence of and risk factors for hepatitis C in haemodialysis patients in Saudi Arabia: a need for a new dialysis strategies	Cross-sectional	KSA	4	43.4	28–58	50.56	100	–	–	1147
40	Soyannwo	1996	Hepatitis C antibodies in haemodialysis and pattern of end-stage renal failure in Gassim, Saudi Arabia	Cross-sectional	KSA/Centre-Gassiem	4	NR	11–80	51.04	100	–	–	96

66	Mitwalli	1997	Aetiology of end-stage renal disease in two regions of Saudi Arabia	Cross-sectional	KSA/Gaizan, Madinah	4	Madinah = 50, Gaizan = 37	37–50	61.41	–	–	–	Madinah = 45, Gizan = 82, Total = 127
46	Al-Homrany	1997	Successful therapy of tuberculosis in haemodialysis patients	Cross-sectional	KSA/South-Abha	3	51.2	25–70	23	100	–	–	270
42	Kumar	1997	Hepatitis C virus infection among haemodialysis patients in the Najran region of Saudi Arabia	Cross-sectional	KSA/South-Najran	3	44.1	16–85	55.31	100	–	–	47
31	Mitwalli	1998	Spectrum of renal osteodystrophy in dialysis patients at a tertiary hospital, Riyadh, Saudi Arabia	Cross-sectional	KSA/Centre-Riyadh	4	42	14–78	50.9	80.7	19.3	–	57
52	Al-Homrany	2001	Psycho-social features of chronic dialysis patients in Saudi Arabia: experience of one centre	Cross-sectional	KSA/South-Abha	3	NR	NR	50	100	–	–	54
43	Khan	2002	A study of end stage renal disease patients from southern part of Arabian peninsula	Cross-sectional	KSA/South-Najran	4	39	13–66	55.22	100	–	–	67
35	Gabr	2004	Cardiac tropinin T and end stage renal disease	Cross-sectional	KSA/Centre-Buraidah	3	NR	27–78	45.2	100	–	–	73
45	Abdelrahman	2006	Tuberculosis in end-stage renal disease patients on haemodialysis	Cross-sectional	KSA/East-Dammam	3	38	21–75	39	100	–	–	256
33	Al-Suwaida	2007	The Gulf survey on anaemia management GSAM 2005	Cross-sectional	GCC	4	53.9	>18	52	100	–	–	563

(Continued)

Table 2
Continued

Ref.	Author	Year	Title	Study design	Location	Quality	Mean of age	Age range	Male %	RRT			ESRD patients
										HD%	PD%	RT%	
51	Al-Shatwi	2007	Nutritional assessment of haemodialysis patients	Cross-sectional	KSA/Centre-Riyadh	4	52	35–69	47.5	100	–	–	61
67	Al-Wakeel	2009	Micro-vascular and Marco-vascular complications in diabetic nephropathy patients referred to nephrology clinic	Cross-sectional	KSA/Centre-Riyadh	3	61.9	19–85	69.6	–	–	–	184
54	Al-Jahdali	2009	Restless legs syndrome in patients on dialysis	Cross-sectional	KSA/Riyadh, Jeddah	4	55.7	39–73	53.7	76.3	23.7	–	114
53	Al-Saran	2009	Nutritional assessment of patients in a large Saudi dialysis unit	Cross-sectional	KSA/Centre-Riyadh	4	50	18–82	54	100	–	–	200

Abbreviations: RRT= renal replacement therapy, HD = haemodialysis, PD= peritoneal dialysis, RT = renal transplantation, ESRD = end-stage renal disease, NR= not reported

Table 3
Summary of reported incidence rate

Ref	*Author*	*Year*	*Location*	*ESRD patients*	*Sample*	*Incidence rate*	*Follow-up time*
23	Shakuntala	1992	UAE/Abudhabi	96	NR	73.6 pmp	14 year
24	El-Reshaid	1994	Kuwait	647	NR	72 pmp	4.5 year
59	Mitwalli	1995	KSA/South-Gizan	124	654685	189.4 pmp	7 month
26	Al-Homrany	1998	KSA/South-Asir	114	NR	214.9 pmp	6 year
27	Subermanian	2001	KSA/South-Gizan	NR	172446	*7.44%	13 year
29	Al-Khunaizi	2003	KSA/East-Dhahran	37	250000	148 pmp	4 year
64	Al-Khunaizi	2007	KSA/East-Dhahran	12	95	**13%	7 year
59	Mitwalli	1995	KSA/West-Madinah	54	828477	65.2 pmp	7 month
61	Mohamed	2004	KSA/West-Madinah	106	NR	137.5 pmp	1 year

* The mean of annual growth rate
** This estimation based on single study per 100 population
NR = not reported, PMP - per million population

Table 4
Summary of reported prevalence

Ref	*Author*	*Year*	*Location*	*ESRD patients*	*Sample*	*Prevalence rate*
14	Ibrahim	1992	KSA	822	5913669	138 pmp
24	El-Reshaid	1994	Kuwait	NR	NR	80.6 pmp
67	Al-Wakeel	2009	KSA/Centre-Riyadh	70	184	*38%

*Prevalence of ESRD among diabetic patients
NR = not reported

Table 5
Summary of reported mortality rate

Ref	*Author*	*Year*	*Location*	*No. of death*	*ESRD patients*	*Mortality rate*	*Follow-up time*
28	Al-Wakeel	2002	KSA/Centre-Riyadh	29	110	*8.07%	5 year
30	Al-Muhanna	1999	KSA/East-Khobar	53	233	22.60%	15 year
29	Al-Khunaizi	2003	KSA/East-Dhahran	NR	37	*8%	4 year
64	Al-Khunaizi	2007	KSA/East-Dhahran	5	95	5.30%	7 year
27	Subermanian	2001	KSA/South-Gizan	NR	393	*9.3%	13 year
63	Mohamed	2005	KSA/West-Madinah	12	94	12.80%	6 month
34	Hussein	1994	KSA/West-Taief	46	325	14%	13 year
24	El-Reshaid	1994	Kuwait	95	647	14.70%	4.5 year

*Annual death rate
NR = not reported

Bahrain[25] and another one was for all the GCC.[33] There were no studies from either Oman or Qatar meeting the inclusion criteria. The majority of studies were either cross-sectional studies (19) or cohort studies (19), and there were 6 case control studies. Only 6 studies of the 44 included studies were given a high score in methodological quality assessment according to NOS because most of the included studies were not reported adequately. Although the other 38 included studies were given a low score, they were included in this review to avoid bias. (Table 2)

Epidemiology of ESRD in the GCC countries

Patient's characteristics

The mean age of participants with ESRD in included studies ranged between 33 and 61.9 years some studies included children (aged <18 years old) but in very small proportion compared to adults, and three studies reported neither the age range of the study population nor mean age.[34–36] In the United Arab Emirates, the highest incidence rate of ESRD was reported in Abu-Dhabi city among the 45–55 years age group,[23] while in Kuwait the median of age among ESRD patients was 45 years.[24] In Saudi Arabia, incidence and prevalence of ESRD are linked directly to increasing age.[19,37] One study conducted in Asir province found that the incidence rate of ESRD is proportional directly to increasing age as follows: the incidence rate of the patients who were aged between 15–44 years is 199.8 pmp, 45–64 years is 577.7 pmp, and >65 years is 716 pmp.[26] The proportion of males for all included studies was slightly higher than females in most included studies. Only four included studies did not report the proportion of male to female study participants. The study population was defined as haemodialysis patients in 24 included studies, and other studies reported the proportion of haemodialysis patients ranged between 52.1% and 97.8%. In two studies, the study population was defined as peritoneal dialysis, while other studies reported the proportion of peritoneal dialysis ranged between 1.2% and 29.1%. Only five studies reported the proportion of renal transplant ranged between 3.7% and 47.9%. (Table 2)

Incidence, prevalence, and mortality rates of ESRD

One study conducted in a general hospital in the United Arab Emirates in Abu-Dhabi city, reported the annual incidence rate of ESRD at 73.6 pmp in 1992.[23] Another population-based study conducted in Kuwait, reported the annual incidence rate of ESRD as 72 pmp in 1994.[24] Six studies were conducted in Saudi Arabia in different regions between 1995 and 2007. It was difficult to track the trend of incidence rate between these studies, but some of them show that the incidence rate seems to be increasing. For example, two studies conducted in Saudi Arabia in Al-Madinah City, demonstrate that the incidence rate had increased from 65.2 pmp in 1995 to 137.5 pmp in 2004;[38,39] while in another region of Saudi Arabia in Gizan, the mean annual growth rate was reported to be 7.44% in the period from 1987 to 2000.[27] (Table 3)

The prevalence rate of ESRD was reported in three studies. Two studies based on national data: one conducted in Kuwait reported the prevalence of ESRD as 80.6 pmp in 1994[24] and another, which was conducted in Saudi Arabia, reported the prevalence of ESRD as 139 pmp in 1986. This latter estimation was based on 29 centres around the kingdom; by geographical region the highest prevalence was found in the central region followed by the eastern region of Saudi Arabia.[19] The most recent study was a single centre study estimating the prevalence of ESRD as 38% among diabetic patients in Riyadh, the capital city of Saudi Arabia.[14] (Table 4)

Mortality rates among ESRD patients were not reported sufficiently either. Most included studies reported the cumulative death events ranging from 5.3% to 22.6%, which were not useful in terms of tracking the trends in mortality rates. Three studies were conducted in Saudi Arabia in different regions, reporting the annual mortality rate as follows: 9.3% in Gizan, 8% in Riyadh and Dharan. These show that mortality rates were not changed in the period between 2001 and 2003.[27–29] (Table 5)

Primary causes of ESRD

Meta-analysis showed that the summarized estimate of diabetic nephropathy (DN) prevalence as

a cause of ESRD is 17.27% (95% CIs, 11.38–26.21%; 21 studies)[30,31,33,39,44–54] and there is no heterogeneity between the studies (I-square = zero%). Subgroup analysis by location shows that the summarized estimate of DN prevalence appears to be higher in urban or more developed areas than rural areas. For instance, in Saudi Arabia the summarized estimate of DN prevalence is 31.41%; (95% CIs, 7.39–133.59; 5 studies)[39,44,53–55] in the western region, 29.15% (95% CIs, 9.21–92.24; 5 studies)[43,48,51,56,57] in the eastern region, and 24.98% (95% CIs, 7.01–88.98; 5 studies)[42,45–47,58] in the central region, compared to 6% (95% CIs, 2–17.8; 3 studies)[36,37,44] in the southern region, which is considered a less developed area. These differences between the areas are not statistically significant (*P*-value = 0.32). Subgroup analysis by period of time shows that the summarized estimate of DN prevalence had significantly increased from 12.38% (95% CIs, 7.38–20.74; 9 studies)[30,31,37,44–46,48,53,58] in the period 1990-1999 to 32.26 (95% CIs, 15.90-65.46; 11 studies)[33,36,39,42,43,47,51,54–57] in the period 2000-2010 with (*P*-value = 0.03).

The summarized estimate of glomerulonephritis prevalence as a cause of ESRD is 12.68% (95% CIs, 8.59-18.70; 21 studies)[30,31,33,36,37,39,42–48,51,53–59] and there is no heterogeneity between the studies (I-square = zero%). Subgroup analysis by locations in Saudi Arabia demonstrate that the highest estimate of glomerulonephritis (GN) prevalence found was in the eastern region (21.67% [95% CIs, 7.74–60.66; 6 studies),[43,48,51,56,57,59] followed by the central region (8.25% [95% CIs, 3.69–18.45; 5 studies])[42,45–47,58] western region (7.97% [95% CIs, 3.11–20.42; 5 studies])[39,44,53–55] and southern region (7.10% [95% CIs, 2.14–23.56; 3 studies]).[36,37,44] These differences between the areas are not statistically significant (*P*-value = 0.39). Also, the heterogeneity in the period of time was explored and demonstrated that the summarized estimate of GN prevalence had declined from 18.82% (95% CIs, 9.65–36.69; 9 studies)[30,31,37,44–46,48,53,58] in the period between 1990–1999 to 10.36% [95% CIs, 6.42–16.70; 11 studies][23–34] in the period between 2000-2010. This difference between these two periods is not statistically significant (*P*-value = 0.15).

The summarized estimate of hypertensive nephropathy prevalence is 7.75% (95% CIs, 6.31–9.52; 17 studies)[18,21,23–27,30,32–39] and there is no heterogeneity between the studies (I-square = zero%). Subgroup analysis by location shows that the highest estimate of hypertensive nephropathy prevalence was found in Saudi Arabia in the central region (20.08% [95% CIs, 6.12–65.89; 5 studies])[24,25,36–38] followed by eastern region (10.56% [95% CIs, 1.80–61.77; 3 studies])[26,27,30] western region (8.13% [95% CIs, 2.95–22.42; 5 studies])[32–35,39] and southern region (4.39% [95% CIs, 1.58–12.1; 2 studies]).[21,35] These differences in the summarized estimates of hypertensive nephropathy prevalence between areas are not statistically significant (*P* value = 0.7). Also, there is no significant difference in the summarized estimate of hypertensive nephropathy prevalence in subgroup analysis by period of time, while the summarized estimate of hypertensive nephropathy prevalence is 7.06% (95% CIs, 3.29–15.16; 7 studies)[18,21,35–39] in the period 1990–1999 and 7.81% (95% CIs, 6.31–9.52; 9 studies)[23–27,30,32–34] in the period 2000-2010 with (*P*-value= 0.8).

Secondary glomerulonephritis/Vasculitis group includes haemolytic ureamic syndrome (HUS) and systematic Lupus erthematosus nephritis (SLE). The prevalence of HUS as a primary cause of ESRD reported at just 1.7% (95% CIs, −0.16–2.74) by one study conducted in Saudi Arabia in eastern region.[30] The summarized estimate of SLE prevalence is 3.61% (95% CIs, 1.88-6.93; 10 studies)[18,24,25,28–31,36,39,40] and the heterogeneity between the studies is high (I-square = 89.2%).

Interstitial Nephritis/Pyelonephritis group including: interstitial nephritis, pyelonephritis, obstructive uropathy, and analgesic abuse. The summarized estimate of interstitial nephritis prevalence is 3.87% (95% CIs, 2.38–6.31; 5 studies)[23,25,30,35,40] with I-square = zero%; obstructive uropathy prevalence is 4.47% (95% CIs, 3.03–6.60; 12 studies)[19,25,26,28,29,31,32,35–38,40] with I-square = zero%; pylonephritis prevalence is 7.45% (95% CIs, 4.81–11.56; 14 studies)[18,19,21,24,28,29,31–33,35–39] with I-square = zero%. Analgesic abuse prevalence was reported in two studies; one study reported the prevalence at 1.8% (95% CIs, [−1.7–5.2][31] and another study reported the prevalence at 2% (95% CIs, 0.1–4).[32]

Cystic/Hereditary/Congenital diseases group includes polycystic kidney disease, medullar cystic disease and congenital/hereditary diseases. The summarized estimate of polycystic kidney

disease prevalence is 4.81% (95% [CIs, 3.05–7.60; 8 studies])[18,28–33,37] with I-square = zero%, and medullar cystic disease prevalence is 1.43% (95% CIs, 0.75–2.72; 3 studies)[18,32,39] with I-square = zero%. While the summarized estimate of hereditary and congenital disease prevalence is 4.43% (95% CIs, 1.74–11.28; 8 studies)[18,25,30,31,35,36,40] with I-square = 83.5%.

The miscellaneous conditions group included ESRD of uncertain aetiology, and other conditions, that are rarely reported as causes of ESRD, such as schistosomiasis, tuberculosis, sickle cell nephropathy and contrast nephropathy. In these conditions for which the aetiology is unknown, the summarized estimate is 19.59% (95% CIs, 11.23–34.17; 17 studies)[18,21,23–26,28–30,32,33,35–40] with I-square = zero, while the summarized estimate for conditions that are rarely reported is 3.45 (95% CIs, 2.04–5.82; 4 studies)[28,36–38] with I-square = zero%.

Co-morbidities associated with ESRD

The chronic disease group included diabetes, hypertension, cardiovascular and vascular disease. Meta-analysis showed that the summarized estimate of diabetes prevalence is 47.85% (95% CIs, 17.47–131.05; 6 studies)[20,23,24,41–43] with I-square = zero%, and hypertension prevalence is 77.88% (95% CIs, 39.76–152.52; 5 studies)[20,23,24,43,44] with I-square = zero%. The summarized estimate of cardiovascular disease prevalence is 14.51% (95% CIs, 5.48–38.45; 6 studies)[25,28,33–36] with I-square = 38.7%. One study reported the prevalence of vascular disease as a co-morbidity condition as 11.7% (95% CIs, 9.1–14.4).[33]

Among the infectious disease group, the most reported and prevalent infectious disease in ESRD patients was hepatitis C virus (HCV), which is more prevalent among haemodialysis patients than among peritoneal dialysis patients. The summarized estimate of HCV prevalence is 48.31% (95% CIs, 29.16–80.04; 10 studies)[29,32,34,37–43] with I-square = zero%, while hepatitis B virus infection 14.82% (95% CIs, 5.22–42.06; 3 studies)[34,40,41] with I-square = zero%, and tuberculosis 6.80% (95% CIs, 4.34–10.67; 5 studies)[34,44–47] with I-square = 13.3%. The prevalence of nasal carriage of staphylococcus aureus, which associated with vascular access related septicaemia, was reported as a co-morbidity condition in HD patients in only two studies conducted in Saudi Arabia in Al-Hafouf City; both reported the prevalence of nasal carriage of staphylococcus aureus as 38% (95% CIs, 7.03–205.41; 2 studies)[48,49] with I-square = zero%. The incidence of peritonitis was reported in only one study as 0.62% among continuous ambulatory peritoneal dialysis patients,[50] while the prevalence is 4.7% (95% CIs, 2.6–6.8).

Other co-morbidities and complication groups included anaemia, bone disease, gastrointestinal abnormalities, liver disease, depression, malnutrition and restless leg syndrome. Meta-analysis showed that the summarized estimate of liver disease prevalence is 12.74% (95% CIs, 6.71–24.2; 3 studies)[28,33,34] with I-square = zero%. The prevalence of anaemia was reported in two studies in this review. One study conducted in Saudi Arabia in Riyadh City, reported the prevalence of anaemia as 47.5% (96% CIs, 35–60.1),[51] while another study reported the prevalence of anaemia for all the GCC countries to be 33.7% (95% CIs, 29.8–37.7).[33] Bone disease was reported in only two studies, both conducted in Saudi Arabia, and reported the prevalence to be 28.9% (95% CIs, 24–33.9) in Taief[31,34] and 70.2% (95% CIs, 58.3–82.1) in Riyadh.[31] The prevalence of depression was reported in two studies. One study conducted in Saudi Arabia in Abha City, reported the prevalence of depression at 59.3% (95% CIs, 46.2–72.4);[52] while another study, which was conducted in Bahrain reported the prevalence of depression among men with ESRD as 48%, which is higher than the level reported among women 42%.[25] The prevalence of malnutrition, restless leg and gastrointestinal abnormalities were reported as 32% (95% CIs, 25.5–38.5), 50% (95% CIs, 40.8–59.2), and 90.7% (95% CIs, 83–98.5), respectively, in three different studies.[53–55]

Causes of mortality in ESRD patients

Meta-analysis showed that the summarized estimate of cardiovascular disease is 36.74 (95% CIs, 8.42–160.36; 6 studies)[23,24,28–30,34] with I-square = zero%, while cerebrovascular disease is 3.68% (95% CIs, 1.25–10.83; 4 studies)[24,28,30,34] with I-square = 14.8%. The summarized estimate of sepsis is 18.97% (95% CIs, 3.14–114.68; 3 studies)[24,30,34] of the deaths in ESRD patients with I-square = zero%. Malfunction of dialysis access

was reported only at one study as a cause of death in ESRD patients at 32% (95% CIs, 17–48).[29] Pulmonary disease (pulmonary infection and pulmonary embolizm), hepatic failure, gastrointestinal bleeding, and malignancy were all given as causes of death in ESRD patients, and death attributed to these causes ranged from 2.1 to 11%.[29,30,34]

Discussion

This review gives an overview of the demographic distribution of ESRD patients in the countries of the GCC. It shows that the overall proportion of males with ESRD is slightly higher than females in most included studies, and the most prevalent age group is between 33 and 60 years old. This is because the proportion of males is higher than females in the general population in Saudi Arabia, where most of the included studies were conducted, while the middle age-group constitute the majority of the population, and the elderly people (those aged >65) constitute only 3%.[4] This clarifies why the proportion of elderly patients with ESRD was small in the included studies in this review.

The majority of ESRD patients in the GCC countries are on haemodialysis. Renal transplantation prevalence was reported in only five studies and ranged between 3.7% and 47.9%.[23,24,27,28,34] However, the most reliable data about renal transplantation in that area is provided by SCOT. This organization coordinates the medical care facilities offered to patients with ESRD and other organ failure; also, it is considered the national authority in laying down the general regulations which relate to all aspects of organ transplantation and brain death in the kingdom. The SCOT 2009 report shows that the number of kidneys transplanted from living donors is more than double the number of kidneys transplanted from deceased donors; the number of kidneys transplanted from living donors has been increasing markedly since 1979. Approximately 40% of ESRD patients had undergone renal transplantation by 2009.[68]

The incidence, prevalence and mortality rate of ESRD in the GCC were not reported sufficiently in this review. All included studies reported the cumulative incidence rate, which does not show changes in the trend; except one study that reported the mean annual growth rate in Gizan was 7.44% in the period from 1987 until 2000.[27] However, two studies in this review that were conducted in Saudi Arabia in Al-Madinah city, show that the incidence rate had increased two-fold from 1988 to 2001.[59,61] This implies that the incidence rate has been increasing gradually over time. Furthermore, mortality rate of ESRD in this review varied widely between studies across the region. That may relate to differing treatment practices which contribute to the variation in outcomes. In addition, it was difficult to track the trend of prevalence and mortality rate in this review because of gaps in the available data. However, SCOT data shows that the incidence rate of haemodialysis patients is increasing annually by 8%,[68] which may imply that the prevalence of ESRD is increasing without taking into account the kidney transplant and mortality rate.

The increasing size of the ESRD population who require RRT in the countries of the GCC might be due to multiple factors such as the rapid socioeconomic development in these countries in recent decades, which has resulted in changing lifestyle and nutrition habits.[8] This in turn plays a role in changing the trend of the prevalence of non-communicable disease such as diabetes, which is globally the leading cause of ESRD.[3] Many reports have provided evidence of increasing prevalence of the most common causes of ESRD in the GCC; such as obesity, hypertension, and diabetes.[7,69,70] The prevalence of diabetes and hypertension is significantly higher in urban populations than rural populations and in men rather than women. This supports the finding in this review that the prevalence of diabetic nephropathy as a cause of ESRD is higher in urban areas than rural areas, but this finding was not statistically significant.

Meta-analysis showed that the leading cause of ESRD in the GCC was diabetic nephropathy 17% followed by GN (13%) and hypertensive nephropathy (8%), while the prevalence of diabetic nephropathy had been increasing significantly over time. Furthermore, among all reported co-morbid conditions in this review, hypertension was the most prevalent chronic condition by 78%. In addition, infectious diseases were also prevalent co-morbid conditions, of which HCV was the most prevalent among ESRD by 48%, especially among haemodialysis patients; which might be due to

frequent attendance of patients at dialysis centres spreading the disease through nosocomial infection[43] and the effect of nurse understaffing.[62] Other factors may increase the risk of HCV, such as the length of dialysis, or the number of blood transfusions; also diabetic patients and males are more likely to develop HCV.[35,44,48,71]

Causes of mortality and hospitalization among ESRD patients usually result from infectious diseases or complications of dialysis, or chronic illness. Among all reported causes of death in ESRD populations in this review, approximately 37% of deaths were related to cardiovascular disease and 19% were related to sepsis. Two studies reported the causes of hospitalization. One study reported the majority cause of hospitalization was cardiovascular disease followed by vascular access related problems, while ischemic heart disease contributed to 19% of the total hospitalization.[28] Another study reported the main cause of hospitalization was vascular access related problems (34%).[63] However, one study suggested that the optimization of arteriovenous fistula (AVF) placement might be a preventative approach to reduce infections associated with vascular access problems, such as staphylococcus aureus infection, which can lead to septicaemia.[49] This suggestion is supported by the National Kidney Foundation's kidney disease outcomes quality initiative (K/DOQI) clinical practice guideline for vascular access, where AVF is the most preferable type for permanent vascular access for HD patients, which related to improved quality of life and increased life expectancy in HD patients.[72]

In comparing this review with a similar publication that was undertaken for the countries of the Middle East,[73] which the countries of the GCC are a part, both highlighted that the incidence of ESRD is increasing substantially and that diabetes is a dominant cause of ESRD. These findings are similar to those reported in the USA and Europe, where diabetes was found to be the dominant cause of ESRD.[74,75] This review indicates that hypertension is the commonest co-morbidity in ESRD population as in the SCOT report.[68] Furthermore, in comparing the findings of this review with the SCOT report, we found that the demographic distribution of age and sex in ESRD are similar. In addition, both show the prevalence of HCV as a co-morbidity to be high: approximately 48% in this review and 26% in the SCOT report, which are higher than those reported in Europe (12%) and the USA (7%).[76]

The strengths of this review are firstly, it includes all of the epidemiological studies conducted in the GCC until 2010. Secondly, this review presents adequate and comprehensive information based on epidemiological studies for multiple outcomes related to ESRD. It provides evidence of the burden of ESRD and defines the high-risk groups; also, it records all co-morbidities and causes of death in ESRD patients in the GCC. This information is extremely valuable for public health planners and administrators to allocate healthcare resources in the countries of the GCC. Furthermore, it gives an overview regarding the sources and quality of the existing health data in the GCC.

Limitations of this review include gaps in the data which did not allow description of trends in the prevalence and mortality rate of ESRD. The majority of included studies in this review were concerned with the haemodialysis population, while there is no available data on either pre-emptive transplantation or elderly people receiving supportive care. In addition, it is prone to a selective bias in terms of excluding all of the patients who received dialysis for less than three months to exclude those patients with acute renal failure. This might result in excluding patients with ESRD who did not survive more than three months. Although this review provided an overview regarding the burden of ESRD in the countries of the GCC, it was not able to provide accurate and current estimates for each related outcome, and the majority of studies were given a low score in quality assessment because they were not well reported. For this reason, the lack of a national renal registry data in the countries of the GCC is a critical issue. Sufficient information is supposed to be recorded for each patient; such as demographic and clinical characteristics, RRT, vascular access, primary causes of ESRD, co-morbidity conditions, laboratory tests, medications, hospitalization, death event and its cause. Each outcome must be recorded by healthcare specialists according to standardized policy, especially in diagnostic procedures.[16] This registry will provide a reliable source of data for further related epidemiological research.

Nevertheless, this review has several important implications for policymakers and public health planners. It provides evidence of the rise in the trend and burden of ESRD in the countries of the GCC; this helps to enable the prediction of healthcare trends. Furthermore, it defined high-risk groups in the GCC population, who were patients with diabetes; this emphasizes the importance of developing potential preventative strategies such as screening programs to detect and manage diabetes and chronic kidney disease (CKD) in early stages and slow down their progression; those programs may be more cost-effective in the future.[3,77] In fact, the quality of care and management should be a target for healthcare providers to improve the quality of life and life expectancy, since hypertension and HCV have become prevalent among ESRD patients and may lead to increased costs of healthcare, because patients with co-morbidities require more hospitalization and medications. In addition, investigating causes of death in patients with ESRD may help to draw the attention of healthcare professionals to specific health issues which can lead to improved healthcare services in that area. This may increase the quality of life and life expectancy of ESRD patients.

Conclusion

This is the first systematic review of the epidemiology of ESRD that has been undertaken in the countries of the GCC. There were several methodological challenges that could not be overcome; however, it was possible to construct a framework of the epidemiology of ESRD in the countries of the GCC. This review presents an overview of the increasing burden of ESRD in the GCC countries, which is similar to the rest of the world. It also provides a list of the major causes of ESRD in these countries and the most frequent morbidities associated with ESRD. Accordingly, this review suggested that the dominant cause of ESRD in the GCC was diabetic nephropathy; and the most frequent co-morbidities were hypertension and HCV. It highlights the emphasis on the need of national renal registry data as a crucial issue and preventative strategies, such as screening programs for the primary causes of ESRD and CKD. Finally, we recommend further epidemiological studies to describe the pattern of the disease in the area and to improve the overall quality of renal care management.

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