

Renal Care in Saudi Arabia:

A Review of the Quality of Healthcare Management

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Amal Abdulaziz Hassanien

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School of Public Health

Abstract

Chronic kidney disease has become a worldwide public health problem as it is linked with an increase in the incidence and prevalence rate of patients with renal failure who require renal replacement therapy with high healthcare costs and poor outcomes. Moreover, chronic kidney disease (CKD) in its earlier stages is associated with a higher prevalence of many adverse outcomes such renal failure, cardiovascular disease, and premature death. In Saudi Arabia, the total number of patients who are receiving renal replacement therapy has been increasing rapidly in recent decades, as the Saudi Centre for Organ Transplantation data has demonstrated, while the estimated annual cost for treating end-stage renal disease uses around 3.8% of the total Ministry of Health's budget in Saudi Arabia. This means that more attention is required for the prevention and management of CKD and its risk factors in Saudi Arabia. Therefore, this thesis was formulated to review the quality of healthcare management for patients with chronic kidney disease in Saudi Arabia. This review was achieved based on: (I) assessing and describing the epidemiology of end-stage renal disease, (II) assessing pre end-stage renal disease care practice, (III) examining the indications for hospital admission among haemodialysis patients. The findings have revealed that the burden of end-stage renal disease has increased substantially in Saudi Arabia particularly among middle-aged diabetic and hypertensive patients, while the most prevalent co-morbid conditions were hypertension and Hepatitis C virus infection. Detecting patients with chronic kidney disease in the earlier stages, and pre end-stage renal disease care practices and its outcomes should be improved in Saudi Arabia. Furthermore, cardiovascular diseases play a major role in increasing the rate of hospitalization and mortality among patients with end-stage renal disease. In conclusion, this review stressed the needs and the importance of multidisciplinary preventive strategies for leading causes of end stage renal disease (ESRD) and improving pre ESRD nephrology care practices and its outcomes in Saudi Arabia. This will not be possible to achieve without collaboration between healthcare providers and a comprehensive national health information system to allow consistent assessment of the quality of healthcare management and provide an updated evidence-based health policy that will help healthcare providers to choose the best intervention that will help to improve healthcare practice outcomes and allocate healthcare resources.

Declaration of Originality

I hereby declare that this thesis and the work reported herein was composed by and originated entirely from me. Information derived from the published and unpublished work of others has been acknowledged in the text and references are given in the list of sources.

(London, 2013)

Amal A. Hassanien

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CHAPTER 1

Introduction

Overview of the healthcare system in Saudi Arabia

Demographic and economic patterns of Saudi Arabia

Demographic patterns

The Kingdom of Saudi Arabia has the largest and fastest growing population among the countries of the Gulf Cooperation Council (1). The recent figures from the population census that was carried out by the Central Department of Statistics and Information (CDSI) in Saudi Arabia in 2012 estimated the population of Saudi Arabia at 29.2 million, with the annual Saudi population growth rate being around 2.9%, with a high density of population in the main cities, particularly Riyadh and Jeddah. Saudi citizens comprise around 68% of the total population, and around 57% of the total population are males (2). A high percentage of the Saudi population are less than 24 years (47.8%) old, while the age group of 25-64 years represents 49.1% of the population. Elderly people who are more than 65 years old represent only 3.1% of the population (1). Estimates based on the census project that the population will reach 37.6 million by 2025 (2) as a result of the high birth rate of 22.5 per 1,000, contrasted with the mortality rate of 3.8 per 1,000 and increased life expectancy of around 72.6 years for men and 76.7 years for females (1). The high percentage of young people and foreign workers in the country will affect the future shape and direction of the Saudi healthcare system (3). Furthermore, the growth of the population address the rapidly increasing demand for essential healthcare services and facilities, and creates more opportunities for healthcare investments (4).

Economic patterns

Saudi Arabia plays a leading role in the Organisation of the Petroleum Exporting Countries (OPEC) and is ranked as the largest producer and exporter of petroleum in the world. Therefore the petroleum sector accounts for around 80% of budget revenues (5, 6). Although the economy of Saudi Arabia is based on oil, in recent decades it has diversified. Currently, Saudi Arabia produces and exports a variety of industrial goods rather than petroleum all over the world (6). The growth in the Saudi economy has had a significant impact on increasing the Saudi community income in recent decades for the per capita Gross Domestic Product (GPD) related to the United States Dollar (US\$) 18,080 in 2003 to US\$ 25,700 in 2012 (2, 7). The Human Development Report 2013 reveals that Saudi Arabia is ranked at a high level (57th in the world) in the Human Development Index (0.78).(8). This improvement in income has had a significant impact in many sectors in the country, including the health sector.

The structure of healthcare services

The Saudi healthcare system consists of: (1) the governmental sector, which provides healthcare services free of charge and includes the Ministry of Health (MOH) and other governmental agencies; and (2) the private sector, which requires out-of-pocket health expenditure and plays a key role in providing quality healthcare services [Figure 1.1]. The Ministry of Health (MOH) in Saudi Arabia is the main provider and funder of healthcare services. It provides 60% of the healthcare services in Saudi Arabia and operates 244 public hospitals with 33,277 beds, along with 2037 primary healthcare centres. Each centre provides healthcare services to an average of 12456 individuals (9). Furthermore, it provides full and free access to all public healthcare services to all citizens and expatriates working within the public sector (10). The other governmental agencies include referral hospitals such as the King Faisal Specialist Hospital & Research Centre, security forces medical services, army forces medical services, National Guard health affairs, Ministry of Higher Education hospitals, ARAMCO hospitals, the Royal Commission for Jubail & Yanbua health services, the school health units of the Ministry of Education and the Red Crescent Society. All these agencies provide all levels of healthcare services to a defined population, who are employees in these agencies and their dependants, except for referral hospitals, the Red Crescent Society and the teaching hospitals. The other governmental hospitals operate 39 hospitals including 10822

beds. The private sector also plays a role in delivering healthcare services particularly in large cities with 125 hospitals including 11833 beds and 2218 dispensaries and clinics (9).

The advancement in healthcare services in Saudi Arabia, as well as other factors, should contribute to improving population health by increasing the institutions of health education and training, with regard to improved life conditions and increased health awareness among the community. However, there is no coordination or any clear communication channels between multidisciplinary healthcare providers such as guidelines of referral from primary to secondary care and health information systems network. This leads to waste of healthcare resources and duplicates the effort of providing healthcare services for the population (4).

The Ministry of Health

Healthcare services in Saudi Arabia have improved remarkably in recent decades in terms of quantity and quality, as they have been given a high priority by Saudi government (3, 11, 12). The MOH, which is also known as the public healthcare system, plays the major role in managing, planning and creating health policies, and supervising health programmes. Also, it monitors healthcare services and advises other governmental agencies and the private sector to achieve the government's health targets (13, 14). The MOH supervises 20 regional directorates general of health affairs all over the country (15), and provides three levels of healthcare services: primary, secondary, and tertiary care (9). Primary healthcare centres provide preventive and curative services, and refer patients that require advanced care to public hospitals, which represent secondary care, while patients who need more complex levels of care are transferred to central or specialised hospitals, which represent tertiary healthcare (4).

However, the MOH has run the centralised management of health services by playing multiple roles including financing, operating, controlling, supervising, and managing the public health sector (4). This current model of healthcare management may not be able to achieve public health targets in the future unless well-planned strategies are undertaken to separate these multiple roles (3, 4, 16). Various feasible strategies were suggested including decentralising management of health services by giving more authority to the regional directorates in terms of planning, recruitment of healthcare professionals, formulating agreements with operating companies, giving some limited financial discretion and

encouraging the privatisation of public hospitals (3, 4). This could help to reduce the annual government expenditure on healthcare services besides producing new financial revenues for the MOH and improving healthcare services and applying the cooperative health insurance scheme (4, 13, 16).

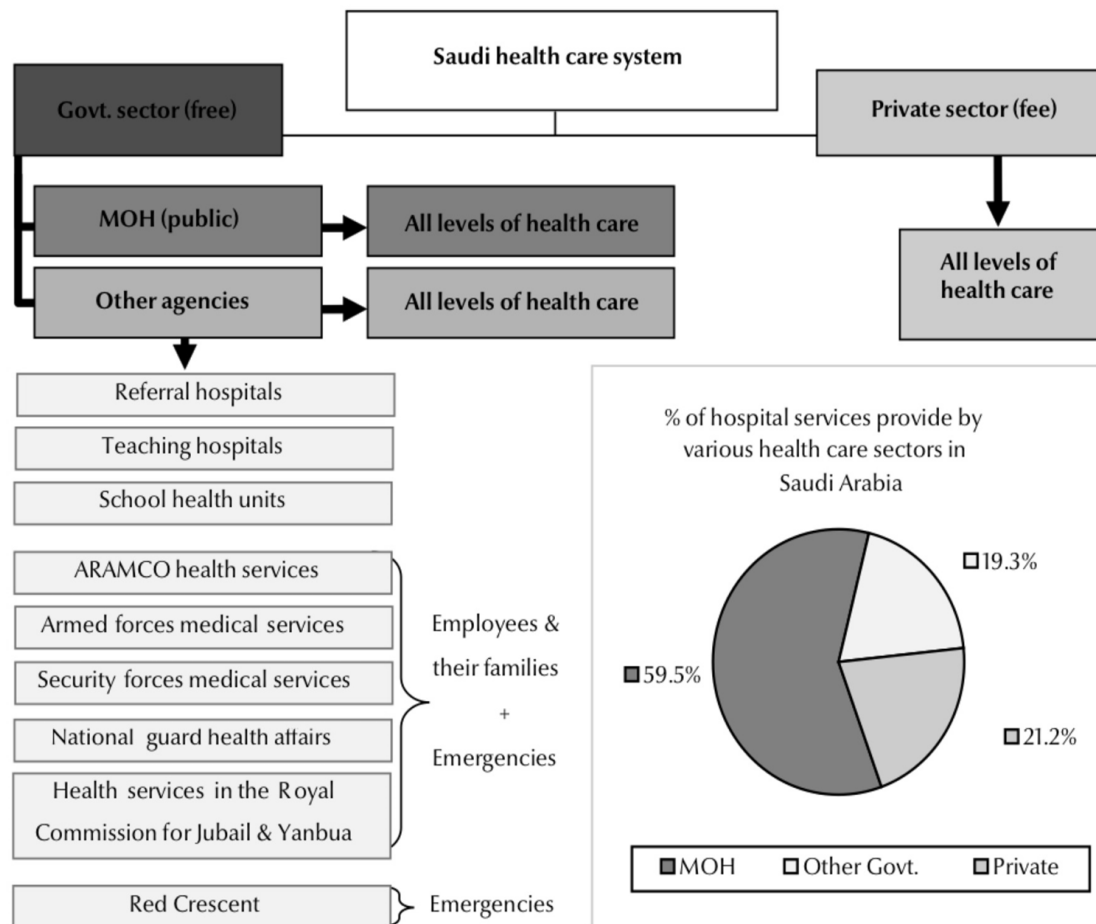


Figure 1.1. The structure of healthcare services in Saudi Arabia (4, 9)

Health workforce

In Saudi Arabia, there is a shortage of national health workers such as physicians, nurses, and pharmacists compared to developed countries and other Gulf Cooperation Council (GCC) countries [Table 1.1] (17). This shortage of healthcare professionals can influence the quality of delivery of healthcare services. Moreover, the majority of the healthcare professionals in the country are expatriates, while Saudis comprise around 38% only of the total health workforce (9). This leads to a very high rate of turnover and instability in the health workforce

(16). Despite the efforts that have been taken by the Saudi government in teaching and training Saudis for healthcare professionals careers, the proportion of the Saudi health workforce is anticipated to decline in the future as a result of the expansion in healthcare facilities around the country (4).

Table 1.1. *Health workforce per 10,000 members of the population in the period between 2005 and 2012 (17)*

Countries	Physicians	Nurses	Pharmacist
GCC countries			
Bahrain	14.9	38.6	2.5
Kuwait	17.9	45.5	3
Oman	20.5	44.9	4.4
Qatar	27.6	73.7	12.6
Saudi Arabia	9.4	21	0.6
United Arab of Emirates	19.3	40.9	5.9
Other countries			
Germany	36.9	113.8	9.5
Japan	21.4	41.4	21.5
United Kingdom	27.7	94.7	6.7
United States	24.2	98.2	8.8

Healthcare finance and expenditure

The public health financing comes mainly from government revenues and the healthcare services are provided free of charge in public healthcare centres in Saudi Arabia. There has been rapid growth in the population and a growing awareness of health issues in the community (3), while the costs of healthcare technology have escalated. Government expenditure on the MOH has increased continuously from 2.8% of the national budget in 1970 (15) to 6% in 2005 and 6.9% with expenditure per capita reaching US\$375 in 2011 (9, 18). However, the World Bank data reveals that the percentage of the total health expenditure in both public and private sectors as a percentage of the GDP of Saudi Arabia in 2011 was 3.7%, which is still behind many developed nations in the world such as the United States (17.9%), United Kingdom and Japan (9.3%), and China (5.2%) (19).

Health insurance in Saudi Arabia

The Council for Cooperative Health Insurance (CHI) was established in 1999 by the government, with its main roles including introducing, regulating, and supervising health insurance strategy for the Saudi healthcare market. In order to meet the growing demands of the population for healthcare services and to ensure the quality of the healthcare services being provided (20), the implementing of CHI scheme is planned to be achieved over three stages. The first stage is to apply CHI to Saudis and non-Saudis who work in the private sector, so that their employers have to pay for covering the healthcare cost of their dependants. The second stage is to apply the CHI to Saudis and non-Saudis who work in the government sectors, while the government have to pay the CHI costs for this category of employee. The third stage is to apply CHI for other groups such as pilgrims to the holy places in Makkah City and Madinah City of Saudi Arabia. To date the first stage has been implemented only, while the government is working systematically to implement the second stage of the CHI for employees in the government sector and the third stage for pilgrims, before privatising the public hospitals. (3, 4)

Accessibility to healthcare services

The recent MOH statistics demonstrate that there is an unsatisfactory distribution of healthcare services and healthcare professionals across the geographical areas of Saudi Arabia (9). Also, many healthcare seekers experience long waiting lists for many healthcare services and facilities (3). There is a lack of healthcare services for disadvantaged groups such as the elderly and disabled people, particularly in rural areas (4). Furthermore, many people such as those who live in the borders and remote areas are not able to access healthcare services (4). However, optimising the accessibility of healthcare services requires equity in allocating the resources of healthcare services and facilities based on the density of the population across the country beside the cooperation between all healthcare sectors in the country (14).

National health information systems (e-health)

The need to develop electronic national health information systems has been increasing in Saudi Arabia. Health information systems have become one of the most challenging and promising fields of research, education, strategic planning and administration to improve the

equability, standards, and the efficiency and quality of healthcare services (21-23). In Saudi Arabia, electronic health information systems have been started up in a number of non-MOH hospitals and organisations such as the King Faisal Specialist hospital and research centre, the National Guard health services, the medical services of the armed forces, and university hospitals. Developing health information system is processed slowly in MOH institutions. Moreover, there are many information systems operating in the regional directorates and in central hospitals which are not connected to each other or to private hospitals or other agencies (24). In order to reinforce the use of e-health strategies and to build up a comprehensive health information system, more coordination is required between different healthcare providers. This will help to prevent the duplication and wasting the resources of healthcare services, and to provide better healthcare practices.

Burden of diseases

The main patterns of disease in Saudi Arabia have changed from communicable to non-communicable diseases and these require more attention from the MOH (10). There is a scarce data in the literature on the increasing prevalence of chronic diseases in Saudi Arabia such as diabetes, hypertension, cardiovascular disease, chronic renal disease, genetic blood disorders, and obesity (25-28). All these diseases are associated with worse health outcomes, complex clinical management, and increased healthcare cost (29). Furthermore, the mortality rate in Saudi Arabia due to non-communicable disease was the highest (644 per 100,000) compared to other causes of mortality, which includes communicable disease (86 per 100,000) and injuries (68 per 100,000) in 2008 (17). Reactive strategies for treating chronic diseases and their complications are costly, and may even be ineffective in certain conditions. For instance, the estimated annual cost of treating diabetes mellitus in Saudi Arabia is US\$1.87 billion (30) while the estimated annual cost for treating end-stage renal disease involves using around 3.8% of the total MOH budget (27). Therefore, a proactive strategy should be the most effective way to reduce the prevalence of chronic diseases and their complications, and thus the associated healthcare costs will be reduced.

The strategy for reforming healthcare system

The MOH has set a strategy to reform the healthcare system and to improve the quality of healthcare services in Saudi Arabia, which was approved by the council of ministers in 2009.

This strategy will be achieved within 20 years. The objectives of the strategy are focused on diversifying funding sources, developing a comprehensive health information system, developing the health workforce, activating the role of MOH in supervising and monitoring healthcare services, encouraging the private sector to help in providing healthcare services, improving the quality of preventive and curative also rehabilitative care, and improving the equity of healthcare service distribution across the country. (4)

Challenges facing healthcare services

Although a huge effort has been undertaken by the MOH to reform the Saudi healthcare system and to improve the quality of healthcare services, many challenges remain. These include tackling the shortages in the health workforce, working with limited financing resources while the population is growing rapidly, the inequity to accessibility of healthcare services across the country, applying the cooperative health insurance scheme to all categories of people, the privatisation of public hospitals, the utilisation of national health information systems and the changing patterns of communicable and non-communicable diseases. (3, 4)

Renal care in Saudi Arabia

Chronic diseases may be prevented sometimes by controlling other related diseases or risk factors. This can improve the quality of life and reduce the utilisation of healthcare services and expenditures. Chronic kidney disease (CKD) is related to many chronic diseases in terms of aetiology and consequences (31). Also, it has a significant impact on the quality of life and productivity (32), and life expectancy (33). Furthermore, the treatment of such disease is costly, particularly if the patient has progressed to the fifth stage of CKD/end-stage kidney disease (estimated glomerular filtration rate (eGFR)= <15mL/min/1.73 m²) and requires renal replacement therapy (RRT) to survive (34, 35).

In Saudi Arabia, the total number of patients who are receiving RRT has been increasing rapidly in recent decades, as the Saudi Centre for Organ Transplantation (SCOT) data has demonstrated [Figure 1.2], with average of annual increase in the dialysis population of around 8% [Figure 1.3] (36). Corresponding to this increase, a rapid expansion has occurred in dialysis facilities from a solitary centre in 1971 to 182 dialysis centres across the country in

2012. A large percentage of these facilities are provided by the MOH, while the non-MOH and private sectors also contribute to providing dialysis facilities (36). This means increasing the demands of healthcare services with limited health resources, which may affect the quality of care. Therefore, attention to both the prevention and management of CKD is required in Saudi Arabia.

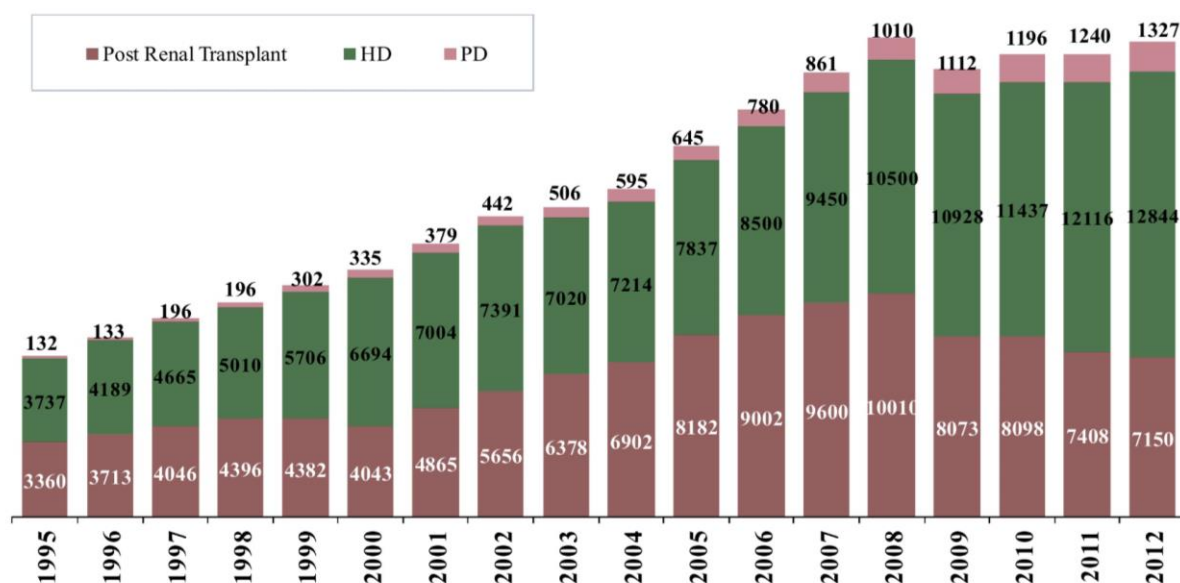


Figure 1.2. The rapid increase of patients who receive renal replacement therapy in Saudi Arabia between 1995 and 2012 (36)

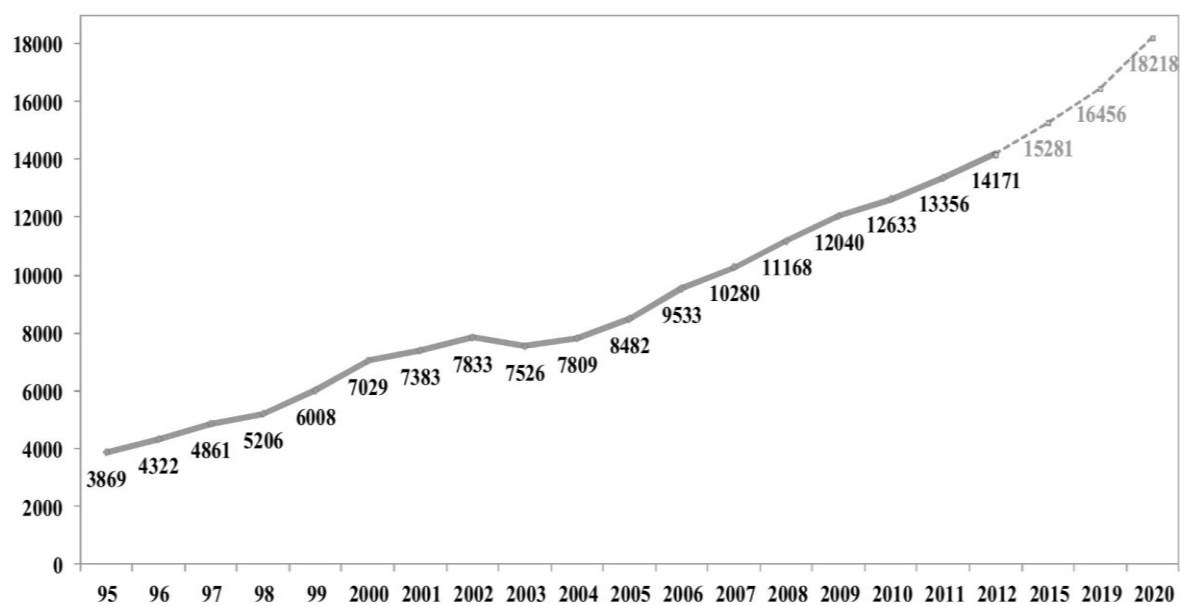


Figure 1.3. Current and projected dialysis population for the period 1995-2020 in Saudi Arabia (36)

CHAPTER 2

Aim and objectives

The aim of this thesis is to review the quality of healthcare management for patients with chronic kidney disease (CKD) in Saudi Arabia, as CKD is associated with worse health outcomes, more complex clinical management, and increased healthcare cost. This review was conducted based on three objectives: the first objective is assessing and describing the epidemiology of end-stage renal diseases to determine the aetiology and the burden of the disease. The second objective is to assess the quality of pre ESRD care and its consequences, as undiagnosed or late detection cases of CKD are associated with an increased incidence rate and burden of ESRD. The third objective is to examine the indications of hospitalisation among haemodialysis patients, which may reflect the severity of patients' co-morbid conditions and the quality of renal care practices, and associated with high healthcare cost.

Objective (1)

Conducting a systematic review and Meta-analysis to assess the results of all relevant epidemiological studies of end-stage renal disease (ESRD) in Saudi Arabia and other Gulf Cooperation Council countries (GCC) up to 2010 to describe the epidemiology of ESRD in these countries based on: the incidence and prevalence of ESRD and the mortality rate in the ESRD population; the distribution of demographic characteristics, and RRT; the aetiology of renal disease; co-morbidity conditions in the ESRD population; and Primary causes of death in the ESRD population. These methods were used because a lack of comprehensive national health information systems 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, or based on small studies. However, analyses of the epidemiology of ESRD itself in this region are also inconsistent. These

conflicting analyses of the epidemiology of ESRD mean that synthesising and assessing the available evidence would be valuable to show the epidemiological pattern of ESRD in Saudi Arabia and other GCC countries. (See chapter 3)

Objective (2)

Conducting a cross-sectional study to assess pre-ESRD care and to investigate the primary causes of ESRD in two of the most active MOH hospitals in the western region of Saudi Arabia after applying for an ethical approval from the Ministry of Health & General Directorate of Health Affairs for data collection. Also, investigating the potential factors that may be associated with late referral to nephrology care and examining its consequences. The participants were prevalent patients in 2011 due to time limitations for collecting data and a lack of national health information systems in Saudi Arabia. A critical data for assessing pre-ESRD care were missing from the medical records such as laboratory and clinical measurements before and at time of initiating dialysis. Therefore, pre-ESRD nephrology care was reviewed based on describing multiple indicators including reasons for referral to nephrology care, referral source to nephrology care, pre-ESRD care period, and vascular access type at the first dialysis. (See chapter 4)

Objective (3)

Conducting a retrospective cohort study in one of the most active MOH hospitals in Makkah City in Saudi Arabia after applying for an ethical approval from the Ministry of Health & General Directorate of Health Affairs for data collection, to examine the indications for hospitalisation among haemodialysis patients by investigating the following: the primary reasons for hospital admissions; and risk factors that increase the number of hospital admissions, and which increase length of stay in hospital. Participants were prevalent patients in 2011 due to time limitations for collecting data and a lack of national health information systems in Saudi Arabia. Each patient was followed-up retrospectively, from the first date of initiating haemodialysis to the end of 2011. This method was used because only two studies in the literature have reported the primary reasons for hospitalisation among the haemodialysis population in Saudi Arabia. The first study conducted in Riyadh City reported cardiovascular disease as the primary reason for hospitalisation (37). The second study

conducted in Al-Madinah City reported vascular access related problems as the primary reason (38). Neither study investigated the risk factors that might increase the rate of hospital admissions or the length of stay in hospital per patient-year on haemodialysis, which could reflect both the severity of patients' co-morbid conditions and the quality of healthcare services. (See chapter 5)

CHAPTER 3

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

Abstract

Background

End-stage renal disease (ESRD) has become a public health problem worldwide, with recent reports showing that the total number of ESRD patients has been growing dramatically. Scarce data are available on the epidemiology of ESRD in the countries of the Gulf Cooperation Council (GCC). In the absence of comprehensive national renal registries in these countries, the data that are available are inaccurate and unreliable. This review was conducted to assess the results of all relevant studies to show the epidemiological pattern of ESRD in the countries of the GCC.

Aims

To describe the epidemiology of ESRD in the countries of the GCC based on: (1) the trends of the incidence and prevalence rate of ESRD, mortality rate in ESRD population, (2) demographic distribution and renal replacement therapy, (3) primary causes of ESRD, (4) co-morbid conditions in ESRD population, (5) causes of mortality in ESRD population.

Methods

A systematic review was conducted by searching Medline and EMBASE databases to identify all relevant papers published up to 2010. The publication references were reviewed to identify any further relevant studies. Two reviewers independently applied the inclusion and exclusion criteria, and carried out data extraction, and quality assessment of studies. Finally, the data related to the incidence, prevalence, mortality rate of ESRD, and demographic

distribution and renal replacement therapy were analysed descriptively, and where possible a meta-analysis was performed to summarise the prevalence of all outcomes related to primary causes of ESRD, co-morbid conditions, and causes of death.

Results

44 studies met the inclusion criteria from the search. This review shows 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 25.9% (95%CI: 20.7%, 31%) with the most prevalent co-morbid conditions being hypertension 66.7% (95%CI: 49.6%, 83.8%) and Hepatitis C Virus infection 41.4% (95%CI: 24.5%, 58.2%); the most common causes of death were cardiovascular disease 44.8% (95%CI: 25.2%, 64.3%) and sepsis 19.6% (95%CI: 12.6%, 26.6%).

Conclusion

This review highlights that the lack of a comprehensive national renal registry data or health information system is a critical issue in the countries of the GCC. The available data also do not provide an accurate and up to date estimate for relevant outcomes. Additionally, considering the increasing burden of chronic kidney disease, these results stress the importance of preventative strategies for leading causes of ESRD. Furthermore, additional studies are needed to describe the epidemiological pattern of ESRD and for assessing the overall quality of renal care to provide an updated evidence-based health policy.

Background

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 (39). 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 (40, 41). ESRD has become a public health concern worldwide, with recent reports showing that the total number of ESRD patients has been growing dramatically. The rising prevalence is due largely to two main factors: the ageing of the population and the global epidemic of diabetes (42-45).

The countries of the Gulf Cooperation Council (GCC), which consist of Saudi Arabia, the United Arab Emirates, Kuwait, Qatar, Bahrain, and Oman, share boundaries and a similar background of culture and ethnicity, while their socio-demographic distributions and socioeconomic development are also similar [Figure 2.1] (46). Although the countries of the GCC have experienced noticeable advances in delivering healthcare, the burden of non-communicable diseases, which generate higher healthcare cost, is increasing rapidly (4, 47). 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 (48), exceeds that in developed countries because of their rapid economic growth and associated changes in lifestyle (26, 49, 50). 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 (51, 52).

The growing incidence of ESRD is increasing the use of RRT, as well as generating greater morbidity, which leads to more hospitalisations (53). ESRD also has a significant effect on quality of life and life expectancy (54, 55). These, in turn, increase healthcare expenditures, placing a heavy financial burden on healthcare funders and general populations to meet the growing needs of patients with ESRD (56-59).

ESRD has a significant effect on public health in the countries of the GCC, as the policy of these countries provides free healthcare services in government hospitals, including RRT to the populations based on clinical need without any restrictions in terms of age, gender, or social status. The majority of RRT facilities are provided by the government sector; therefore, any increase in its use would be associated with a significant increase of healthcare expenditures.

Scarce data are available on the epidemiology of ESRD in the countries of the GCC. In the absence of health information systems or a comprehensive national renal registry data 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 (60), 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, which was a period when risk factors for the disease became more common; this might be due to underreporting the cases of ESRD (61, 62), or might be influenced by mortality and renal transplant rate. Other studies report

inconsistent results of primary causes of ESRD (57, 63). These conflicting analyses of the epidemiology of ESRD mean that synthesising and assessing the available evidence would be valuable to show the epidemiological pattern of ESRD in the countries of the GCC.



Figure 3.1. The countries of the Gulf Cooperation Council map (64)

Aims and scope

This review was conducted to assess the results of all relevant epidemiological studies of ESRD in the countries of the GCC up to 2010 to describe the epidemiology of ESRD in these countries based on:

- The incidence, prevalence rate of ESRD, and mortality rate in ESRD population
- The distribution of demographic characteristics, and RRT
- The aetiology of renal disease
- Co-morbid conditions in the ESRD population
- Primary causes of death in the ESRD population.

Methods

Systematic review

Searching

A systematic review was conducted by searching the Ovid database, which included Medline and EMBASE databases, to identify all relevant papers published between 1950 and 2010 without any restrictions on the language of publications, 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* [Appendix A]. Additionally, the reference lists of all identified papers were reviewed to locate other studies, which were not identified in the database search.

Selection criteria

Inclusion criteria

Study design and principal outcomes

Any observational epidemiological study, including cohort studies, case-control studies, cross-sectional studies, and ecological studies, reporting ESRD incidence, prevalence, primary causes, co-morbid conditions, and mortality rate /causes were included in this review.

Defining population and setting

All of the studies that have been included defined the study population to have ESRD or 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.

Exclusion criteria

Studies where the study population mainly comprised children, or pregnant woman, or patients on dialysis without mentioning the dialysis period or a period less than three months were excluded, to avoid including patients with acute kidney disease. In addition, studies that used qualitative methods or epidemiological studies that did not report any statistical information about any relevant outcomes were excluded.

Data abstraction and validity assessment

All potential relevant publications, which were obtained from searching databases, their titles and abstracts 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 selection criteria above. Studies that met the inclusion criteria for the review had data extracted. Data relating to study design, setting, definition of outcome measures, inclusion and exclusion criteria of the study population, methodological quality using the Newcastle Ottawa Scale (NOS) (65) and outcomes were then independently extracted by two reviewers using standardised data extraction form [Appendix B]. In the methodological quality assessment NOS, the included studies were classified after aggregating the score as follows: scores of six or higher were chosen to indicate higher methodological quality, a score less than six indicates a lower methodological quality.

Data analyses

The extracted data for patients' characteristics, prevalence, incidence, and mortality rate of ESRD were analysed descriptively.

Quantitative data synthesis

The outcomes, primary causes, co-morbid conditions, and causes of mortality were classified for analyses. Primary causes of ESRD were classified as in the ICD9-CM code (66) into the following categories: diabetes, glomerulonephritis (GN), secondary GN/vasculitis, interstitial nephritis/pyelonephritis, hypertension/large vessel disease, cystic/hereditary/congenital diseases, neoplasms/tumours, and miscellaneous conditions. Co-morbid conditions were classified into three groups: chronic diseases including diabetes, hypertension, cardiovascular disease; infectious diseases including hepatitis C virus (HCV), hepatitis B virus (HBV), tuberculosis (TB), catheter-related infection, and peritonitis; and other co-morbid conditions included anaemia, bone disease, gastrointestinal abnormalities, liver disease, depression, malnutrition, and restless leg syndrome. Mortality causes were classified into cardiovascular disease, cerebrovascular disease, sepsis, malfunction of dialysis access, pulmonary disease, including pulmonary infection and pulmonary embolism, hepatic failure, gastrointestinal bleeding, and malignancy.

The data related to primary causes, co-morbid conditions, and causes of death were entered into STATA version 11 for statistical analysis. These data then were used to conduct meta-analysis to summarise the estimate of the prevalence for each outcome where possible. The degree of heterogeneity was assessed between the studies statistically using meta-analysis to obtain an I-square value (67). 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 and methodological and statistical variation of the studies. To account for the anticipated heterogeneity, the DerSimonian and Laird model random effect method was used to combine the effect size (68, 69). Subgroup analysis was performed when it was necessary and possible 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 (95% CIs)) were calculated where meta-analysis was not appropriate to conduct for any outcome, especially for those that were reported in less than three studies.

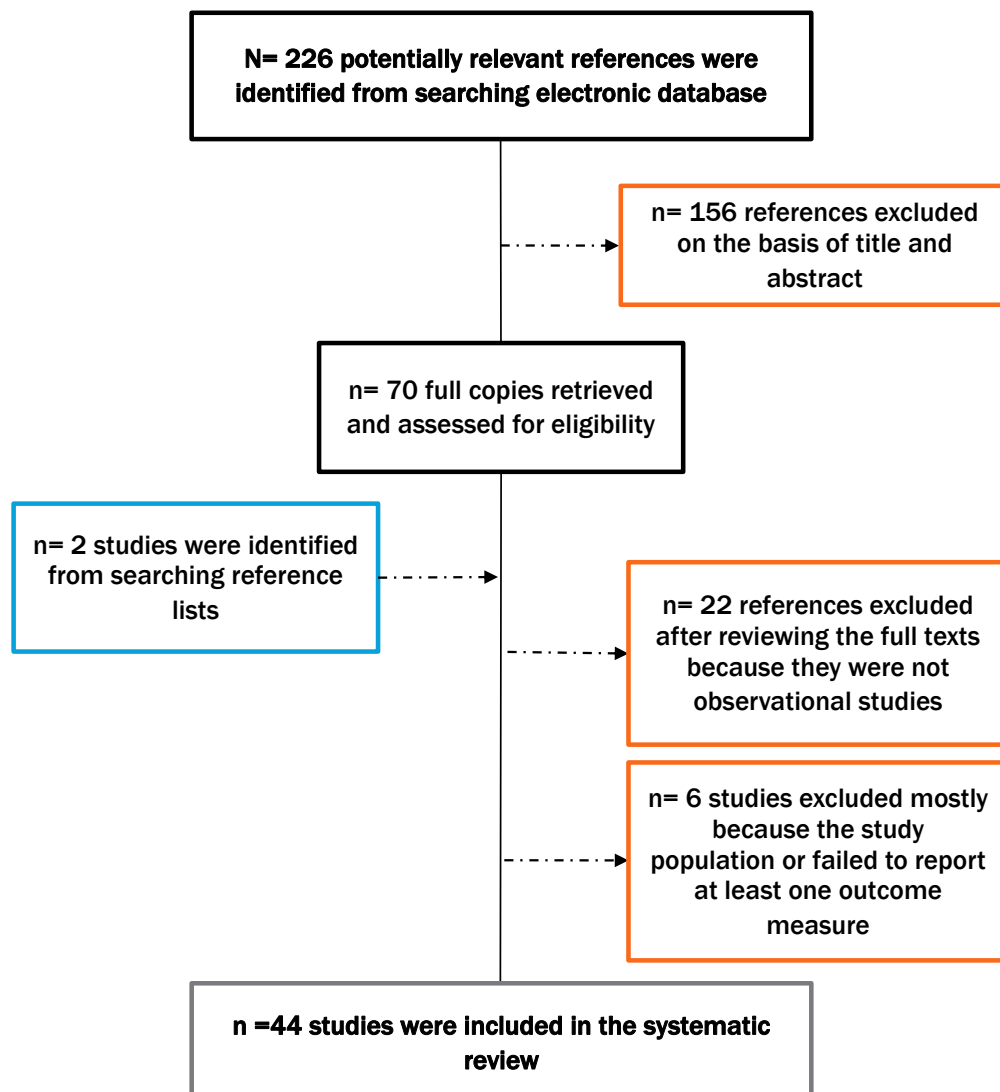
Results

The search identified 226 articles published from 1950 up to 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) (70) and Al-Shohaib (1999) (71) were excluded because, although the study population was defined as dialysis patients, no further background was provided such as the dialysis period, so the study may have included patients with acute renal failure. Al-Mohaya (1990) (72), Yahya (1998) (73), Rafi (2007) (74) and Al-Jahdali (2009) (75) were excluded because no relevant statistical outcomes were reported [Table 2.1]. After the search inclusions and exclusions, 44 epidemiological studies were eligible for the systematic review [Figure 2.2].

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 (76), one was conducted in Kuwait (77), one was conducted in Bahrain (78), and another one included the entire GCC (79). 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 11 studies of the 44 included 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 33 included studies were given a low score, they were included in this review to avoid bias [Table 2.2].



Nine (9) studies reported incidence rate, three (3) studies reported prevalence rate, eight (8) studies reported mortality rate, twenty-one (21) studies reported primary causes of ESRD, thirty-one (31) studies reported co-morbid conditions in patients with ESRD, and six (6) studies reported causes of mortality in ESRD.

Figure 3.2. A flow chart shows a summary of the systematic review

Table 3.1. *Summary of excluded studies*

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

Table 3.2. Summary of included studies

Ref	Author	Year	Title	Study design	Location	Quality	Sample Size	Mean of age	Age range	Male %	RRT		
											HD%	PD%	RT%
(80)	Hussein	1990	Tuberculosis in patients undergoing maintenance dialysis	Cohort	KSA/ West-Taief	4	205	42	20-60	26	62.4	13.17	—
(81)	Hussein	1990	Chronic intermittent peritoneal dialysis using automatic cyclor machine	Cross-sectional	KSA/ West-Taief	1	28	NR	6 -74	42	—	100	—
(82)	Fakunle	1991	Prevalence of antibodies to hepatitis C virus in haemodialysis patients in Riyadh	Cross-sectional	KSA/ Centre-Riyadh	3	190	40.4	15 -75	63.2	100	—	—
(61)	Ibrahim	1992	End-stage renal disease (ESRD) in Saudi Arabia	Cross-sectional	KSA	2	822	NR	NR	50.7	98	2	—
(76)	Shakuntala	1992	End-stage renal disease in native population of the United Arab Emirates	Cohort	UAE/ Abu Dhabi	4	96	45	11 - 75	NR	52.1	—	47.9
(83)	Al-Nasser	1992	Seropositivity to hepatitis C virus in Saudi haemodialysis patient	Case control	KSA/ South-Baha	5	66	46	30-68	53.81	100	—	—
(84)	Mitwalli	1992	Hepatitis C in chronic renal failure patients	Case-control	KSA/ Centre-Riyadh	2	30	NR	NR	NR	86.6	13.3	—
(77)	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	647	NR	NR	63.7	75.1	21.2	3.7
(85)	Hussein	1994	Observations in Saudi Arabian dialysis population over a 13-year period	Cross-sectional	KSA/ West-Taief	4	325	43	6-89	53.84	63.8	1.2	35
(86)	Mitwalli	1995	The incidence of End-stage renal disease in two regions of the Kingdom of Saudi Arabia	Cohort	KSA/ Gaizan, Madinah	7	Madinah= 108, Gaizan= 187, Total=295	NR	11-75	61	—	—	—

Ref	Author	Year	Title	Study	Location	Quality	Sample	Mean of	Age range	Male %	RRT		
(87)	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	1147	43.4	28-58	50.56	100	–	–
(88)	Soyannwo	1996	Hepatitis C antibodies in haemodialysis and pattern of end-stage renal failure in Gassim-Saudi Arabia	Cross-sectional	KSA/ Centre-Gassim	4	96	NR	11-80	51.04	100	–	–
(89)	Mitwalli	1997	Aetiology of end-stage renal disease in two regions of Saudi Arabia	Cross-sectional	KSA/ Gaizan, Madinah	4	Madinah=45, Gizan=82, Total=127	Madinah=50, Gaizan=37	37 -50	61.41	–	–	–
(90)	Al-Homrany	1997	Successful therapy of tuberculosis in haemodialysis patients	Cross-sectional	KSA/ South-Abha	3	270	51.2	25-70	23	100	–	–
(91)	Kumar	1997	Hepatitis C virus infection among haemodialysis patients in the Najran region of Saudi Arabia	Cross-sectional	KSA/ South-Najran	3	47	44.1	16- 85	55.31	100	–	–
(92)	Al-Ghamdi	1998	Whole blood total, reduced and oxidised ascorbic acid levels in Saudi patients with chronic renal failure: influence of gender and chronic haemodialysis	Case-control	KSA/ Centre-Riyadh	4	55	33	23-43	50.98	100	–	–
(93)	Al-Homrany	1998	Incidence of treated end-stage renal disease in Asir region, southern Saudi Arabia	Cohort	KSA/ South-Asir	8	114	47.89	9 - 99	56.1	–	–	–
(94)	Mitwalli	1998	Spectrum of renal osteodystrophy in dialysis patients at a tertiary hospital-Riyadh- Saudi Arabia	Cross-sectional	KSA/ Centre-Riyadh	4	57	42	14 -78	50.9	80.7	19.3	–
(95)	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	233	45.5	34-57	65.6	100	–	–

Ref	Author	Year	Title	Study	Location	Quality	Sample	Mean of	Age range	Male %	RRT		
(96)	Suberamani an	2001	Haemodialysis utilisation in a single centre dialysis unit_ in the Kingdom of Saudi Arabia	Cohort	KSA/ South-Gizan	4	393	40.7	10 - 93	46.6	86.5	_	13.5
(97)	Youbissi	2001	CAPD in Dammam Central Hospital_ Saudi Arabia: a Five year experience	Cohort	KSA/East-Dammam	3	31	41.3	10 - 85	32.25	_	100	_
(98)	Al-Homrany	2001	Psycho-social features of chronic dialysis patients in Saudi Arabia: experience of one centre	Cross-sectional	KSA/ South-Abha	3	54	NR	NR	50	100	_	_
(37)	Al-Wakeel	2002	Morbidity and mortality in ESRD patients on dialysis	Cohort	KSA/ Centre-Riyadh	4	110	53.8	17 - 92	64.5	59.1	29.1	11.8
(99)	Shaheen	2002	Pre-End stage chronic renal failure: the Jeddah kidney centre experience	Cohort	KSA/ West-Jeddah	6	99	49.5	11 - 90	58.6	_	_	_
(100)	Khan	2002	A study of end stage renal disease patients from southern part of Arabian peninsula	Cross-sectional	KSA/ South-Najran	4	67	39	13 - 66	55.22	100	_	_
(78)	Al-Haddad	2003	Depression among end stage renal disease patients	Case control	Bahrain	4	45	52	NR	46.7	100	_	_
(101)	Saxena	2003	The susceptibility of patients with type-2 diabetes to hepatitis C virus infection during long-term haemodialysis	Cohort	KSA/East-Hafouf	7	196	52.8	14 - 84	50.51	100	_	_
(102)	Saxena	2003	The prevalence of Nasal carriage of <i>Staphylococcus aureus</i> and associated vascular access-related septicaemia among patients on haemodialysis in Al-Hasa region of Saudi Arabia	Cohort	KSA/East-Hafouf	3	208	47.5	15 - 84	45.7	100	_	_
(103)	Al-Khunaizi	2003	End stage renal disease experience in a general hospital in eastern Saudi Arabia	Cohort	KSA/East-Dhahran	4	37	60	NR	50	97.8	2.2	_

Ref	Author	Year	Title	Study	Location	Quality	Sample	Mean of	Age range	Male %	RRT		
(104)	Al-Mueilo	2004	Gastro-duodenal lesions and Helicobacter pylori infection in haemodialysis patients	Case control	KSA/East-Khobar	3	54	NR	16-85	59	100	–	–
(105)	Mohamed	2004	Incidence and aetiology of end-stage renal disease in Madinah Munawarah Area: Any changing trends?	Cohort	KSA/West-Madinah	5	106	NR	>13	61.6	–	–	–
(106)	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	198	47	15-84	54	100	–	–
(107)	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	198	47	15-84	54	100	–	–
(108)	Saxena	2004	Advancing age and the risk of nasal carriage of <i>Staphylococcus aureus</i> among patients on long-term hospital-based haemodialysis	Cohort	KSA/East-Hafouf	6	205	NR	15-84	46.8	100	–	–
(109)	Gabr	2004	Cardiac tropinin T and end stage renal disease	Cross-sectional	KSA/Centre-Buraidah	3	73	NR	27-78	45.2	100	–	–
(110)	Mohamed	2005	Morbidity and mortality in ESRD patients on regular haemodialysis: a single centre experience	Cohort	KSA/West-Madinah	4	395	51	13-85	58.5	100	–	–
(111)	Abdelrahman	2006	Tuberculosis in end-stage renal disease patients on haemodialysis	Cross-sectional	KSA/East-Dammam	3	256	38	21-75	39	100	–	–
(79)	Al-Suwaida	2007	The Gulf survey on anaemia management GSAM 2005	Cross-sectional	GCC	4	563	53.9	>18	52	100	–	–
(112)	Al-Khunaizi	2007	Patterns of renal pathology among renal biopsy specimens in eastern Saudi Arabia	Cohort	KSA/East-Dhahran	6	95	41	23-59	55	–	–	–
(113)	Al-Shatwi	2007	Nutritional assessment of haemodialysis patients	Cross-sectional	KSA/Centre-Riyadh	4	61	52	35-69	47.5	100	–	–

Ref	Author	Year	Title	Study	Location	Quality	Sample	Mean of	Age range	Male %	RRT		
(114)	Al-Ali	2008	Increased prevalence of glycoprotein IIb/IIIa Leu33Pro polymorphism in end stage renal disease patients on haemodialysis	Case-control	KSA/East-Dammam	7	42	50	38-65	68	100	–	–
(115)	Al-Wakeel	2009	Micro-vascular and Marco-vascular complications in diabetic nephropathy patients referred to nephrology clinic	Cross-sectional	KSA/Centre-Riyadh	3	184	61.9	19-85	69.6	–	–	–
(116)	Al-Jahdali	2009	Restless legs syndrome in patients on dialysis	Cross-sectional	KSA/Riyadh-Jeddah	4	114	55.7	39-73	53.7	76.3	23.7	–
(117)	Al-Saran	2009	Nutritional assessment of patients in a large Saudi dialysis unit	Cross-sectional	KSA/Centre-Riyadh	4	200	50	18-82	54	100	–	–

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

Epidemiology of ESRD in the GCC countries

Patient's characteristics

Demographic distribution

The arithmetic mean of the mean age of participants with ESRD in included studies in the review is 47 years old (standard deviation (SD) = ± 6.4); some studies included children (aged <18 years old) but in a very small proportion compared to adults, while three studies reported neither the age range of the study population nor the mean age. In the United Arab Emirates, the highest incidence rate of ESRD was reported in Abu-Dhabi city among the 45-55 years age group (76) while the median age among ESRD patients was 45 years in Kuwait (77). In Saudi Arabia, many studies conducted in the 1990s showed that the incidence and prevalence of ESRD were linked directly to increasing age (70, 87). One study conducted in the Asir province showed that the incidence of ESRD is directly proportional to increasing age as follows: the incidence rate of the patients who aged between 15-44 years is 199.8 per million population (pmp), 45-64 years is 577.7 pmp, and >65 years is 716 pmp (93). The arithmetic mean of the proportions of males for all included studies in the review is 52.3 (SD= ± 9.9), which is slightly higher than the proportion of females 47.4 (SD= ± 9.8). Only two included studies did not report the proportion of male to female study participants [Table 2.2].

Renal replacement therapy

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 that the proportion of peritoneal dialysis ranged between 1.2% and 29.1%. Only five studies reported the proportion of renal transplant ranging between 3.7% and 47.9%. Haemodialysis treatment was clearly the dominant RRT followed by renal transplantations and peritoneal dialysis [Table 2.2].

The incidence rate 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 (76); another population-based study conducted in Kuwait reported the annual incidence rate of ESRD as 72 pmp in

1994 (77). Six studies were conducted in Saudi Arabia in different regions between 1995 and 2007. It was difficult to track the trend of the 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 (86, 105), 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 (96) [Table 2.3].

The prevalence rate of ESRD

The prevalence rate of ESRD was reported in three studies. Two studies were based on national data: one was conducted in Kuwait and reported the prevalence of ESRD as 80.6 pmp in 1994 (77); the other was conducted in Saudi Arabia and 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 (61). The most recent study was a single centre study estimating the prevalence of ESRD as 38% among diabetic patients in Riyadh City in Saudi Arabia (115) [Table 2.4].

Mortality rate among ESRD patients

Mortality rate was not reported sufficiently either. Most included studies reported the cumulative death events ranging from 5.3% to 22.6%, which was not useful in terms of tracking the trends in mortality rates. However, it might reflect the variety of quality of healthcare services between healthcare centres. Three studies were conducted in Saudi Arabia in different regions reporting the annual mortality rate as follows: 9.3% in Gizan, and 8% in Riyadh and Dharan. These show that mortality rates did not change significantly in the period between 2001 and 2003 (96, 103, 118). Also, the reported mortality rate in those studies might be underestimated as some deaths outside hospitals might not have been reported [Table 2.5].

Table 3.3. Summary of reported incidence rate

Ref	Author	Year	Location	ESRD patients	Sample	Incidence rate	Time intervals
(76)	Shakuntala	1992	UAE/Abudhabi	96	NR	73.6 pmp	14 year
(77)	El-Reshaid	1994	Kuwait	647	NR	72 pmp	4.5 year
(86)	Mitwalli	1995	KSA/South-Gizan	124	654685	189.4 pmp	7 month
(93)	Al-Homrany	1998	KSA/South-Asir	114	NR	214.9 pmp	6 year
(96)	Subermanian	2001	KSA/South-Gizan	NR	172446	*7.44%	13 year
(103)	Al-Khunaizi	2003	KSA/East-Dhahran	37	250000	148 pmp	4 year
(112)	Al-Khunaizi	2007	KSA/East-Dhahran	12	95	**13%	7 year
(86)	Mitwalli	1995	KSA/West-Madinah	54	828477	65.2 pmp	7 month
(105)	Mohamed	2004	KSA/West-Madinah	106	NR	137.5 pmp	1 year

* The mean annual growth rate,

** This estimation was based on a single study per 100 population, NR=not reported

Table 3.4. Summary of reported prevalence

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

*Prevalence of ESRD among diabetic patients, NR=not reported

Table 3.5. Summary of reported mortality rate

Ref	Author	Year	Location	Death	ESRD patients	Mortality rate	Time intervals
(119)	Al-Wakeel	2002	KSA/Centre-Riyadh	29	110	*8.07%	5 year
(95)	Al-Muhanna	1999	KSA/East-Khobar	53	233	22.60%	13 year
(103)	Al-Khunaizi	2003	KSA/East-Dhahran	NR	37	*8%	4 year
(112)	Al-Khunaizi	2007	KSA/East-Dhahran	5	95	5.30%	7 year
(96)	Subermanian	2001	KSA/South-Gizan	NR	393	*9.3%	13 year
(110)	Mohamed	2005	KSA/West-Madinah	12	94	12.80%	6 month
(85)	Hussein	1994	KSA/West-Taief	46	325	14%	13 year
(77)	El-Reshaid	1994	Kuwait	95	647	14.70%	4.5 year

* Annual death rate, NR=not reported

Primary causes of ESRD

Diabetic nephropathy

Meta-analysis results showed that the summarised estimate of diabetic nephropathy (DN) prevalence as a cause of ESRD in the countries of the GCC was 25.87% (95%CI: 20.69%, 31.05%) and the heterogeneity between the studies was high (I-square= 91.5%). Subgroup analysis by period of time shows that the summarised estimate of DN prevalence had significantly increased from 16.93% (95%CI: 13.01%, 20.84%; I-square= 68.9%) in the period 1990-1999 to 32.91 (95%CI: 27.70%, 38.13%; I-square= 80.2%) in the period 2000-2010 [Figure 2.3]. Subgroup analysis by location shows that the summarised estimate of DN prevalence appears to be higher in urban or more developed areas than rural areas. For instance, in Saudi Arabia the summarised estimate of DN prevalence is 32.20% (95%CI: 23.99%, 40.40%; I-square= 63.5%) in the western region, 30.97% (95%CI: 23.99%, 37.95%; I-square= 73.95%) in the eastern region, and 25.09% (95%CI: 15.78%, 34.40%; I-square= 83.3%) in the central region compared to 13.72% (95%CI: 4.29%, 23.15%; I-square=67.4%) in the southern region, which is considered a less developed area [Figure 2.4] [Table 2.6].

Hypertensive nephropathy

The hypertension and large vessel disease group included renal vascular disease and nephrosclerosis, which occurred as a result of severe blood pressure. The summarised estimate of hypertensive nephropathy prevalence in the countries of the GCC is 13.52% (95%CI: 9.36%, 19.01%) and the heterogeneity between the studies was high (I-square= 91.9%). Subgroup analysis by period of time showed that the prevalence of hypertensive nephropathy has not changed in the last two decades, while the summarised estimate of hypertensive nephropathy prevalence is 12.94% (95%CI: 6.45%, 19.44%; I-square= 93.3%) in the period 1990-1999 and 14.18% (95%CI: 9.36%, 19.01%; I-square= 83.2%) in the period 2000-2010 [Figure 2.5]. Subgroup analysis by location shows that the highest estimate of hypertensive nephropathy prevalence was found in Saudi Arabia in the central region 23.60% (95%CI: 12.80%, 34.40%; I-square= 89.1%), followed by western region 12.67% (95%CI: 5.35%, 19.98%; I-square= 79.3%), eastern region 12.55% (95%CI: 3.61%, 21.49%; I-square= 56%) and southern region 4.45% (95%CI: 1.57%, 7.34%; I-square= zero%) [Figure 2.6] [Table 2.7].

Glomerulonephritis

The summarised estimate of glomerulonephritis prevalence as a cause of ESRD in the countries of the GCC is 18.77% (95%CI: 14.19%, 23.35%) and the heterogeneity between the studies was high (I-square= 92.6%). Subgroup analysis by period of time showed that the summarised estimate of GN prevalence had declined from 24.53% (95%CI: 15.93%, 33.13%; I-square= 93.3%) in the period 1990-1999 to 13.95% (95%CI: 9.56%, 18.34%; I-square= 87.4%) in the period 2000-2010 [Figure 2.7]. Subgroup analysis by location in Saudi Arabia demonstrated that the highest estimate of GN prevalence found in eastern region 27.68% (95%CI: 16%, 39.36%; I-square= 92.7%), followed by the central region 15.74% (95%CI: 7.93%, 23.55%; I-square= 85.6%), southern region 14.16% (95%CI: -0.28%, 28.59%; I-square= 94.2%) and western region 8.02% (95%CI: 5.38%, 10.67%; I-square= 0%) [Figure 2.8] [Table 2.8].

Secondary glomerulonephritis/Vasculitis

This group includes haemolytic uremic syndrome (HUS) and Systemic Lupus Erythematosus (SLE) nephritis. The prevalence of HUS as a primary cause of ESRD was reported as just 1.3% (95%CI: 0.27%, 3.72%) by one study conducted in Saudi Arabia in the eastern region. The summarised estimate of SLE prevalence is 4.39% (95%CI: 2.78%, 6%) and the heterogeneity between the studies was high (I-square=65.6%) [Figure 2.9] [Table 2.9].

Interstitial Nephritis/Pyelonephritis

This group included interstitial nephritis, pyelonephritis, obstructive uropathy, and analgesic abuse. The summarised estimate of interstitial nephritis prevalence is 4.09% (95%CI: 1.52%, 6.67%) with high heterogeneity (I-square= 80.1%) [Figure 2.10]. Pyelonephritis prevalence is 10.72% (95%CI: 4.82%, 16.62%) with high heterogeneity (I-square= 96.3%) [Figure 2.11]; and obstructive uropathy prevalence is 4.93% (95%CI: 3.51%, 6.35%) with moderate heterogeneity (I-square= 59.3%) [Figure 2.12]. Analgesic abuse prevalence was reported in two studies: one study reported the prevalence at 1.7% (95%CI: -0.04%, 9.4%) (94) and another study reported the prevalence at 2% (95%CI: 0.56%, 5.1%) (101) [Table 2.10].

Cystic/Hereditary/Congenital diseases

This group includes polycystic kidney disease, medullary cystic disease, and congenital/hereditary diseases. The summarised estimate of polycystic kidney disease prevalence is 3.56% (95%CI: 2.77%, 4.36%) with an I-square of 0% [Figure 2.13], medullary

cystic disease prevalence is 1.53% (95%CI: 0.56%, 2.50%) with an I-square of 0% [Figure 2.14], while the summarised estimate of hereditary and congenital disease prevalence is 5.03% (95%CI: 2.28%, 7.77%) with high heterogeneity (I-square=87.3%) [Figure 2.15] [Table 2.11].

Miscellaneous

This group of conditions included ESRD of uncertain aetiology (unknown), and other conditions that are rarely reported as causes of ESRD, such as schistosomiasis, TB, sickle cell nephropathy, and contrast nephropathy. For these conditions, for which the aetiology is uncertain, the summarised estimate is 20.96% (95%CI: 14.89%, 27.04%) with high heterogeneity (I-square= 94.9%), and subgroup analysis by period of time showed that reporting the aetiology of renal disease has not improved in the last two decades as the summarised estimate of reporting the cause of ESRD as uncertain aetiology did not change significantly from the period 1990-1999 to the period 2000-2010 [Figure 2.16]. The summarised estimate for conditions that are rarely reported is 2.37% (95%CI: 1.07%, 3.68%) with an I-square of 73.8% [Figure 2.17] [Table 2.12].

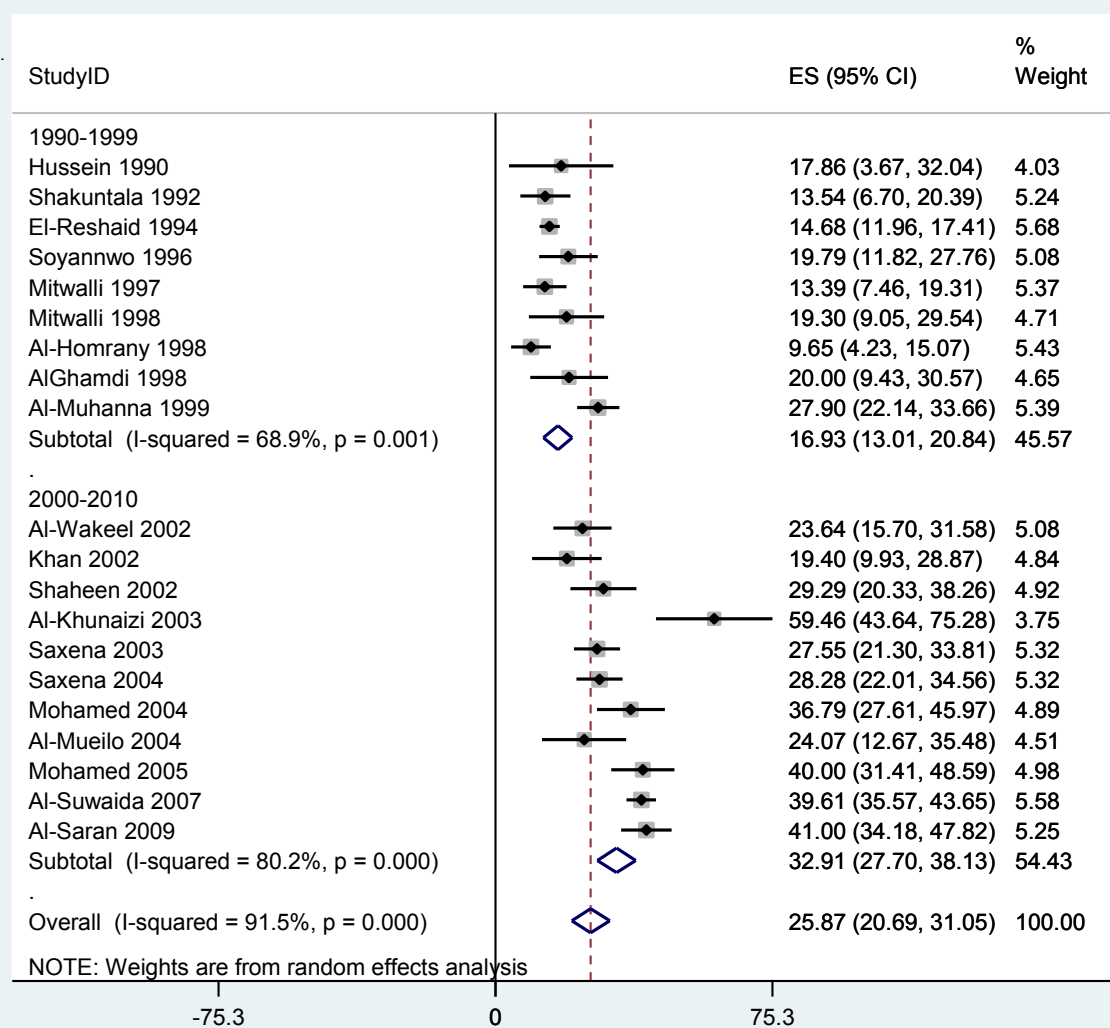


Figure 3.3. Forest plot showing the pooled estimate and subgroup analyses by time of the prevalence of diabetic nephropathy as a cause of ESRD in the countries of the GCC.

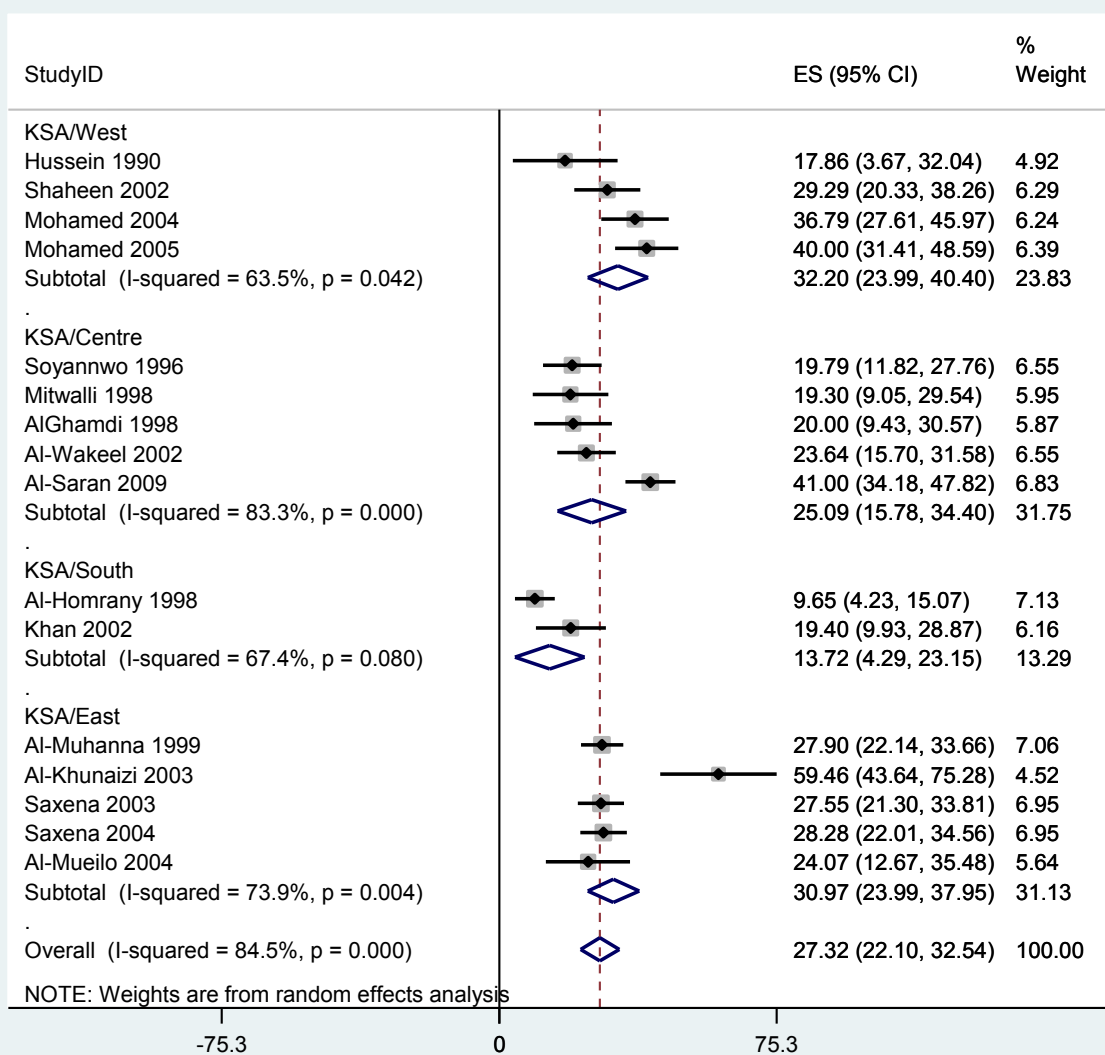


Figure 3.4. Forest plot showing the pooled estimate and subgroup analyses by locations of the prevalence of diabetic nephropathy as a cause of ESRD in Saudi Arabia.

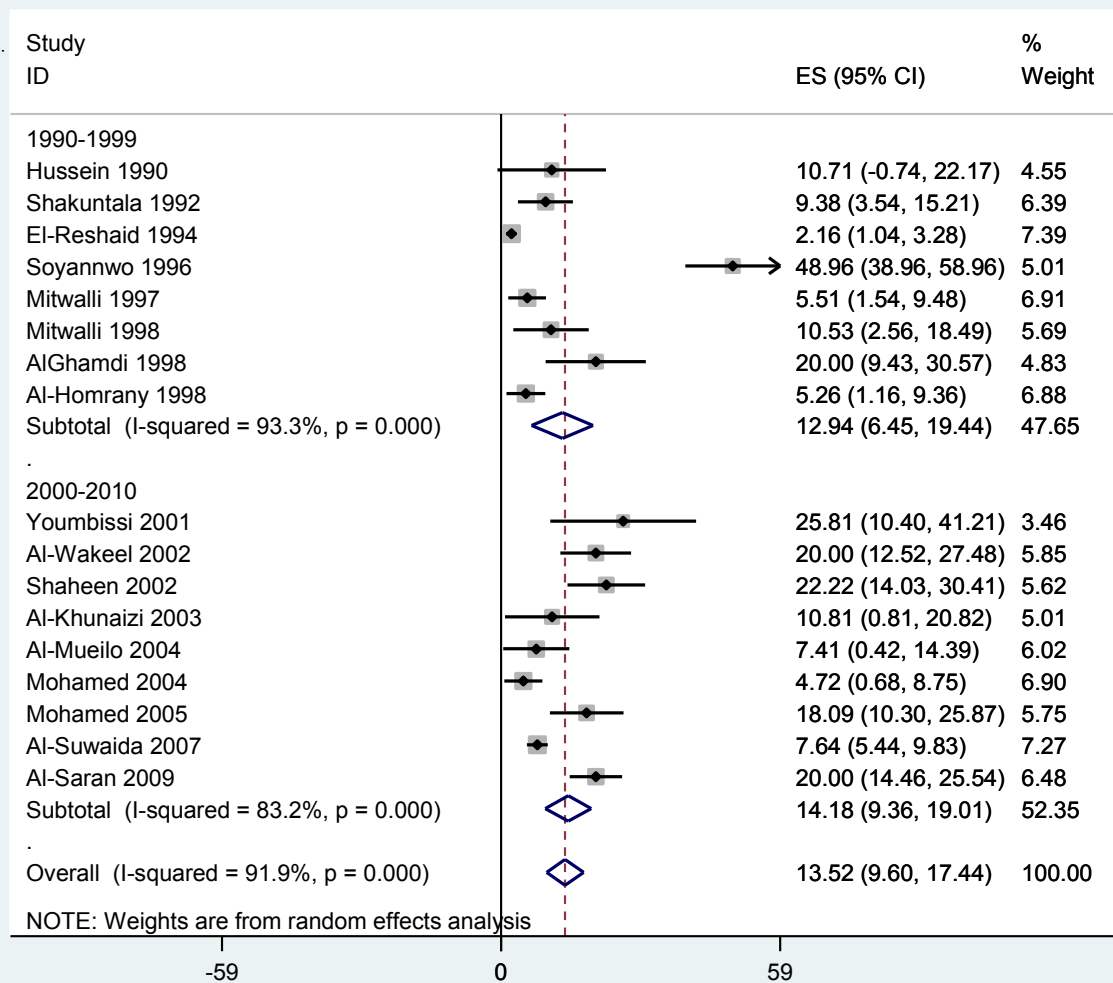


Figure 3.5. Forest plot showing the pooled estimate and subgroup analyses by time of the prevalence of hypertensive nephropathy as a cause of ESRD in the countries of the GCC.

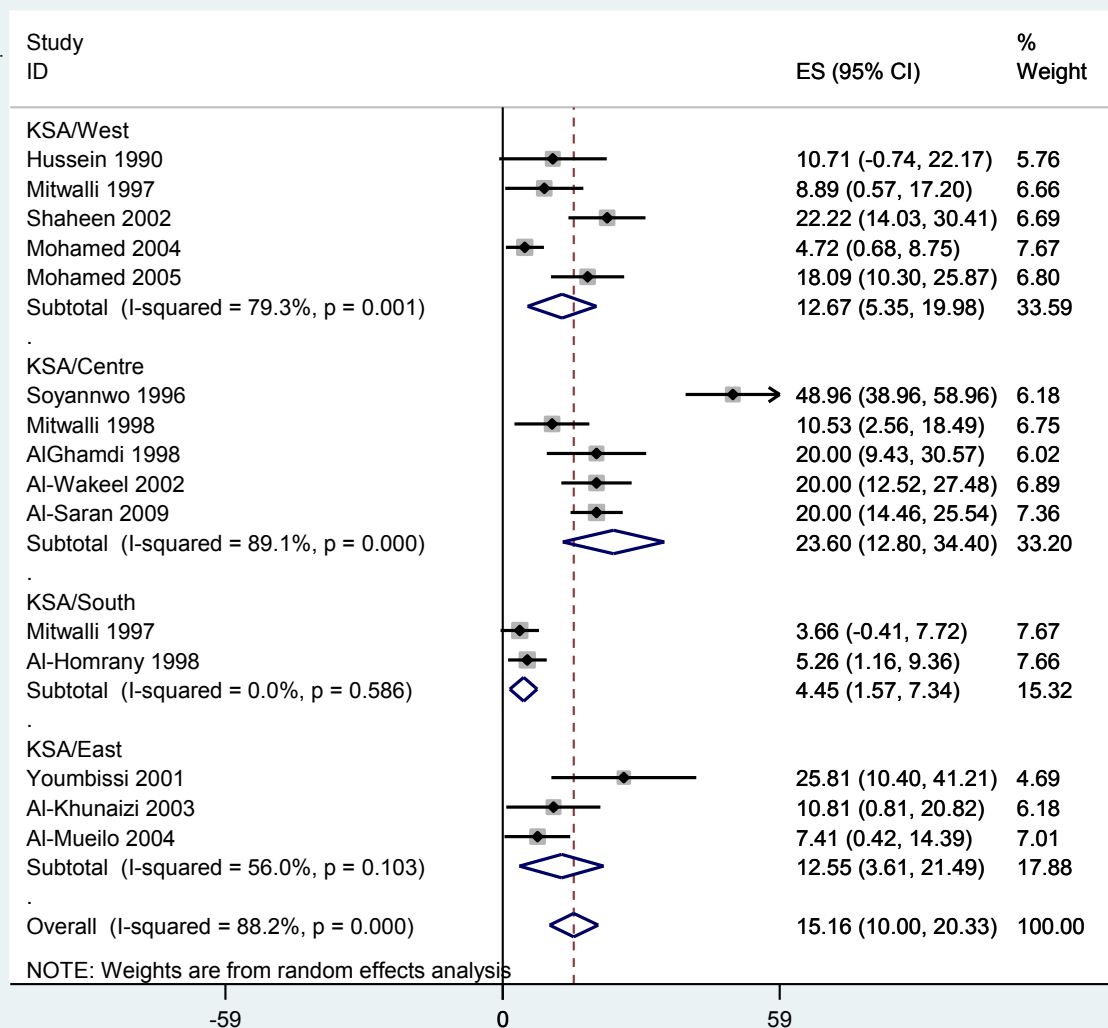


Figure 3.6. Forest plot showing the pooled estimate and subgroup analyses by location of the prevalence of hypertensive nephropathy as a cause of ESRD in Saudi Arabia.

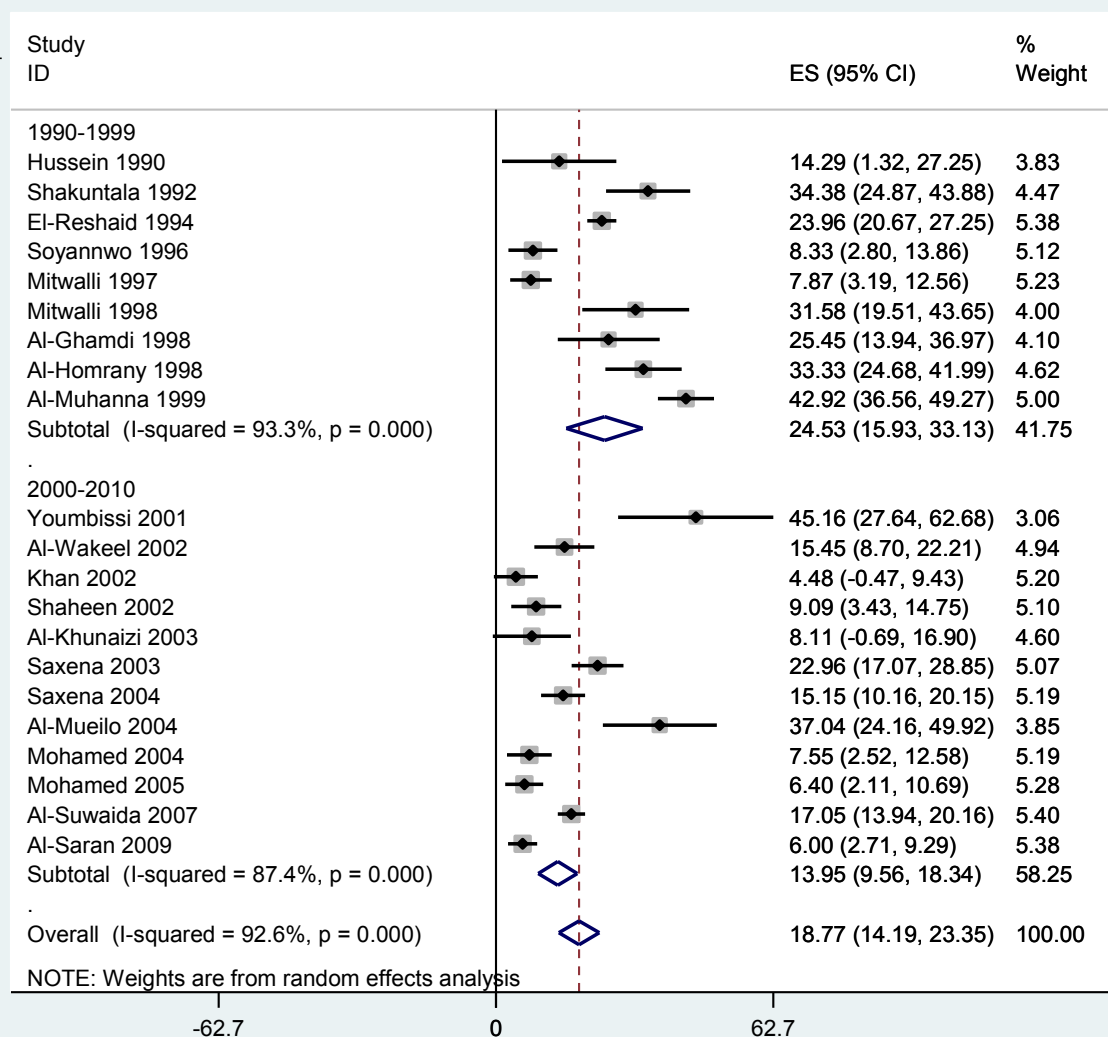


Figure 3.7. Forest plot showing the pooled estimate and subgroup analyses by time of the prevalence of glomerulonephritis as a cause of ESRD in the countries of the GCC.

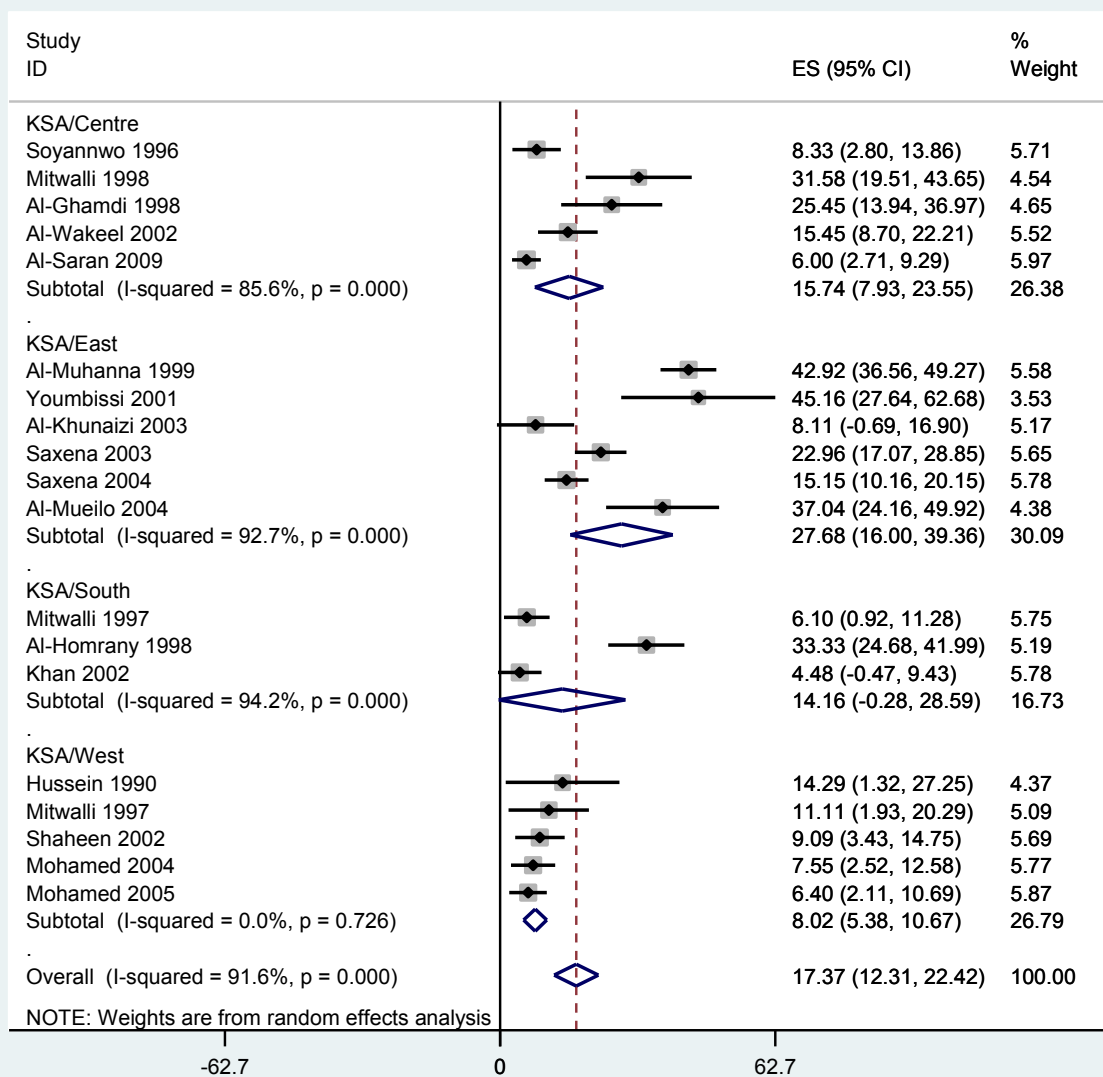


Figure 3.8. Forest plot showing the pooled estimate and subgroup analyses by location of the prevalence of glomerulonephritis as a cause of ESRD in Saudi Arabia.

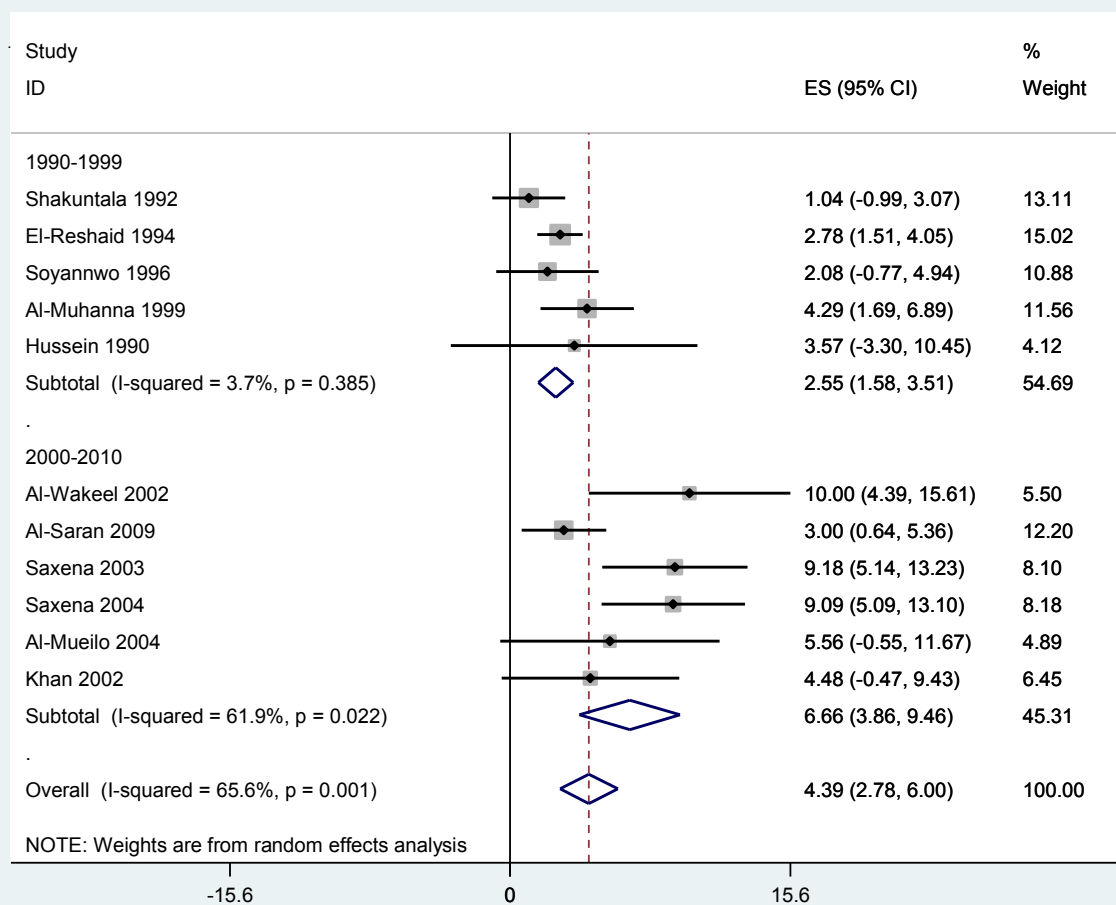


Figure 3.9. Forest plot showing the pooled estimate and subgroup analyses by time of the prevalence of Systemic Lupus Erythematosus as a cause of ESRD in the countries of the GCC.

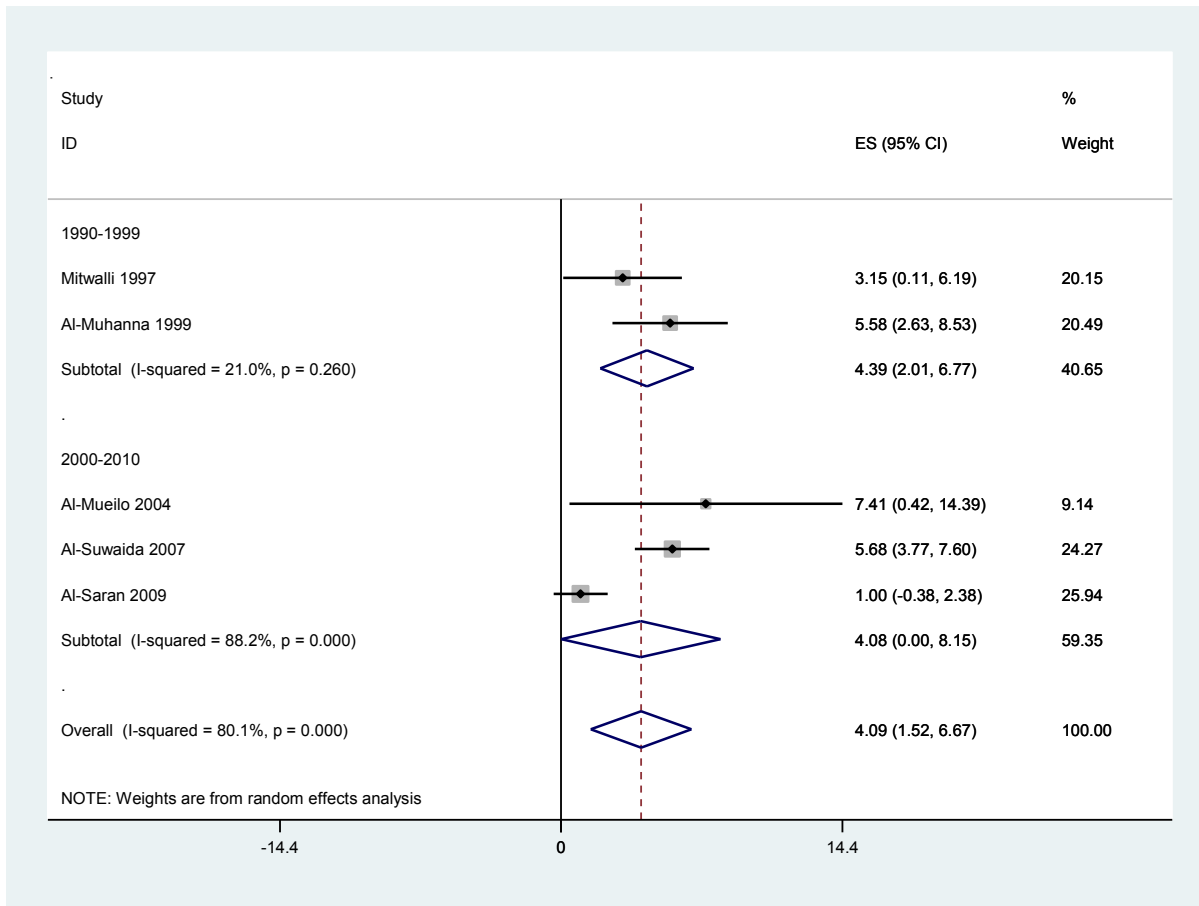


Figure 3.10. Forest plot showing the pooled estimate and subgroup analyses by time of the prevalence of interstitial nephritis as a cause of ESRD in the countries of the GCC.

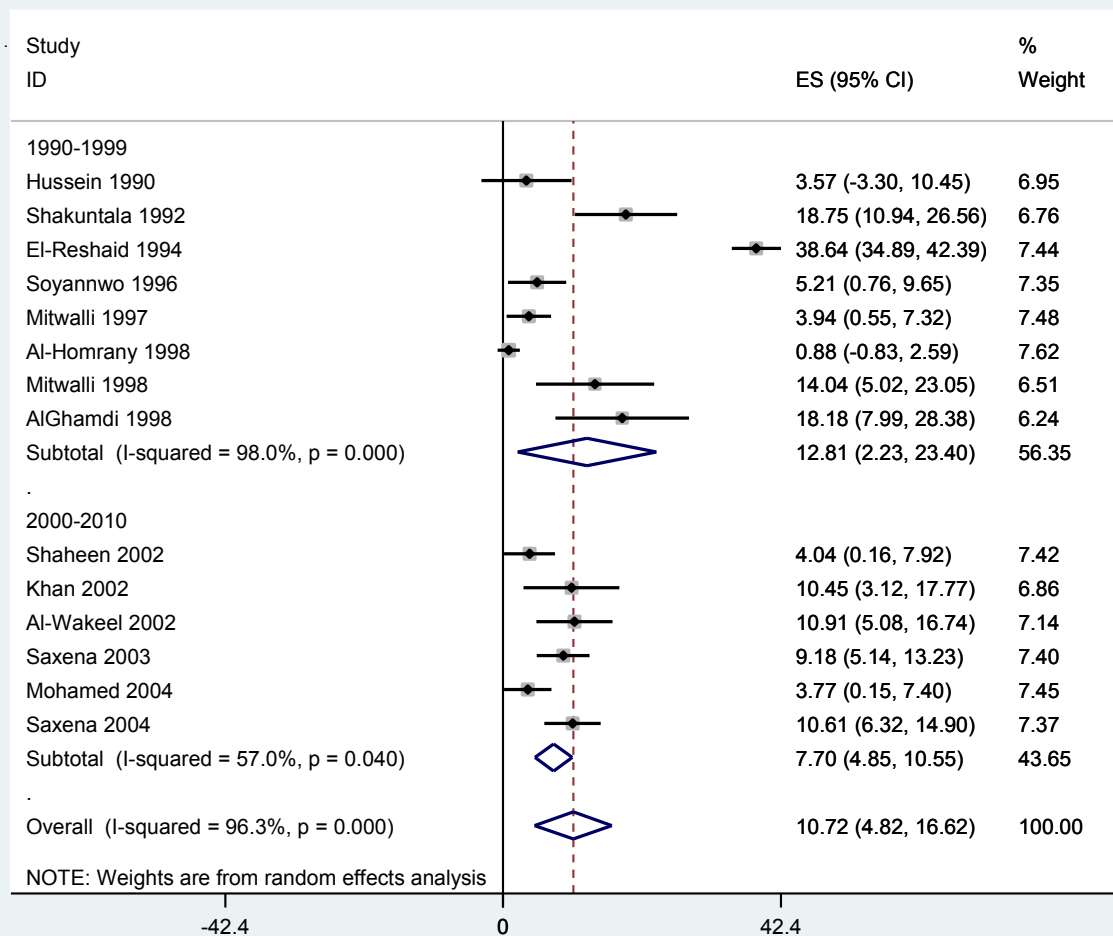


Figure 3.11. Forest plot showing the pooled estimate of the prevalence of pyelonephritis as a cause of ESRD in the countries of the GCC.

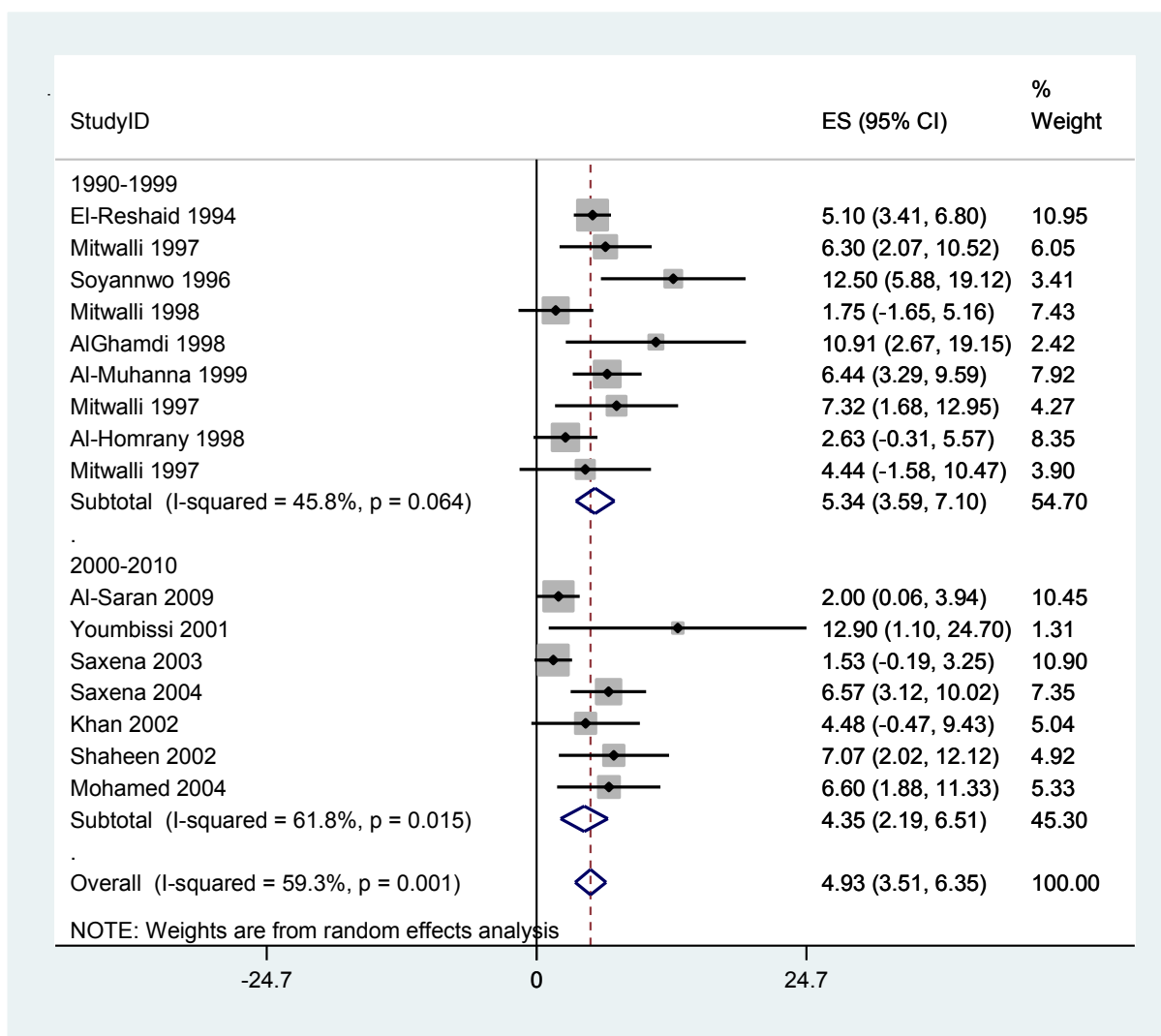


Figure 3.12. Forest plot showing the pooled estimate the prevalence of obstructive uropathy as a cause of ESRD in the countries of the GCC.

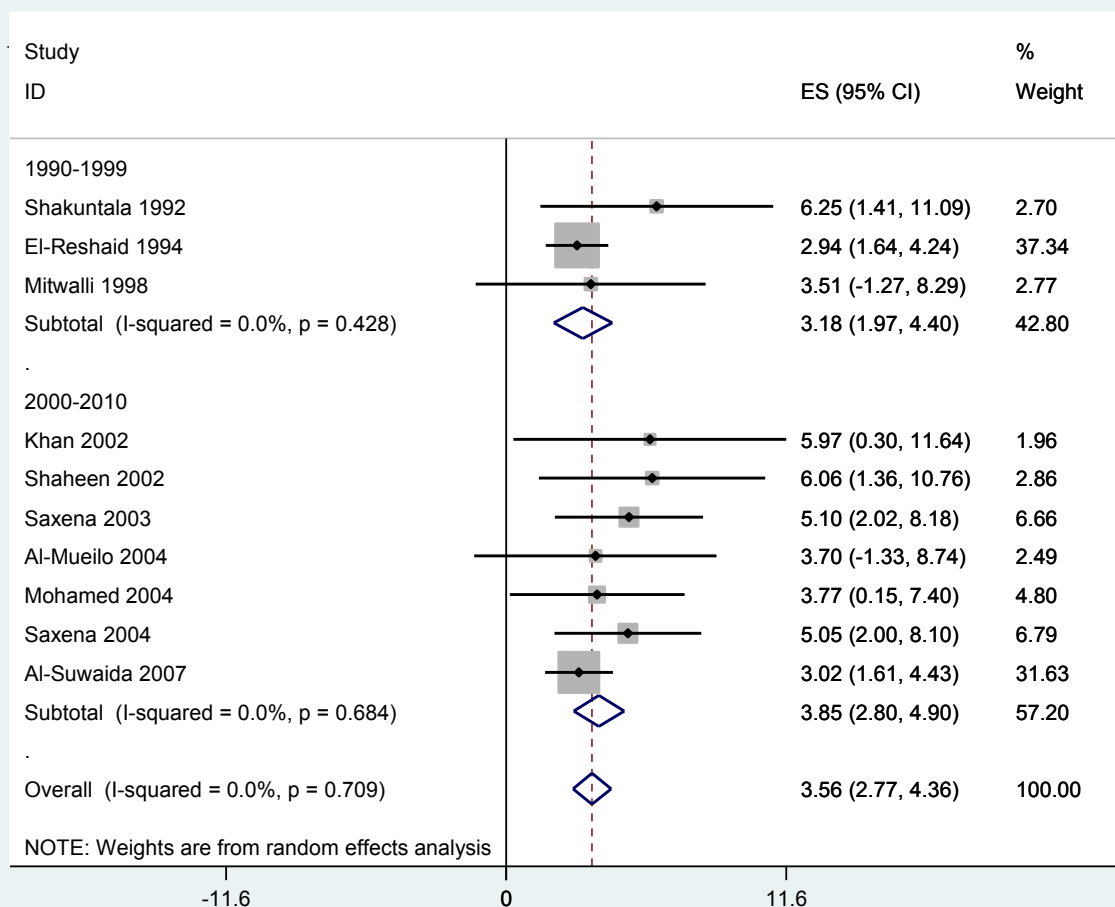


Figure 3.13. Forest plot showing the pooled estimate of the prevalence of polycystic kidney as a cause of ESRD in the countries of the GCC.

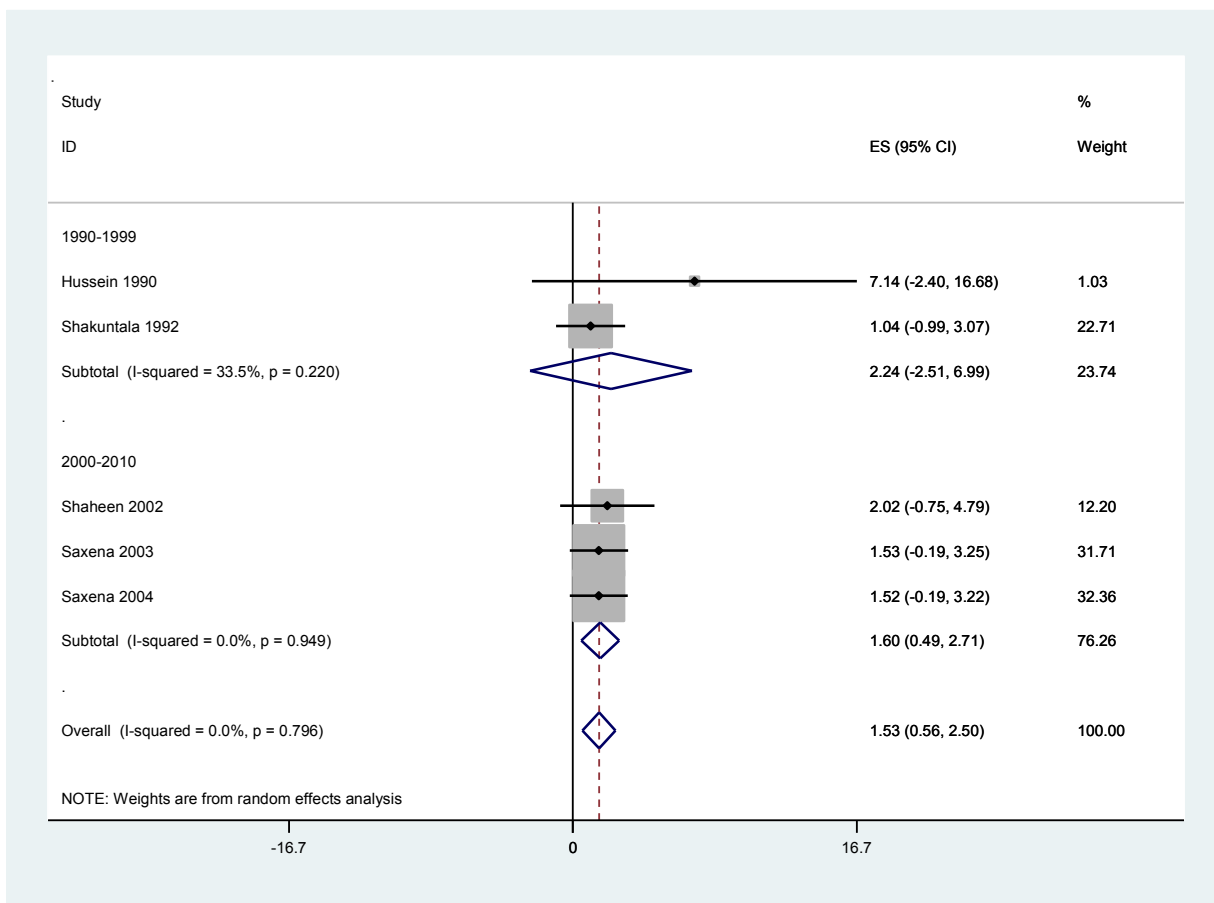


Figure 3.14. Forest plot showing the pooled estimate of the prevalence of medullary cystic disease as a cause of ESRD in the countries of the GCC.

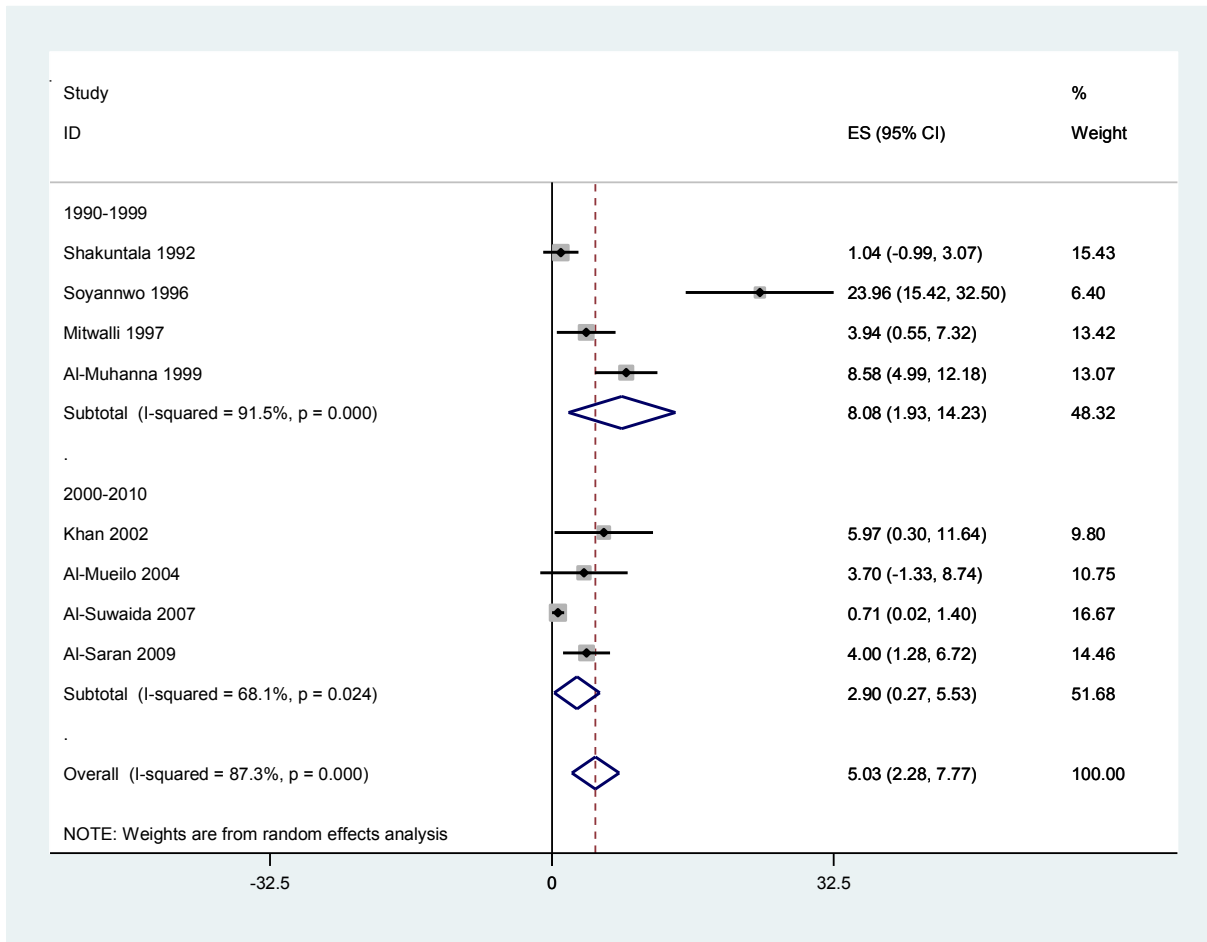


Figure 3.15. Forest plot showing the pooled estimate of the prevalence of congenital/hereditary diseases as a cause of ESRD in the countries of the GCC.

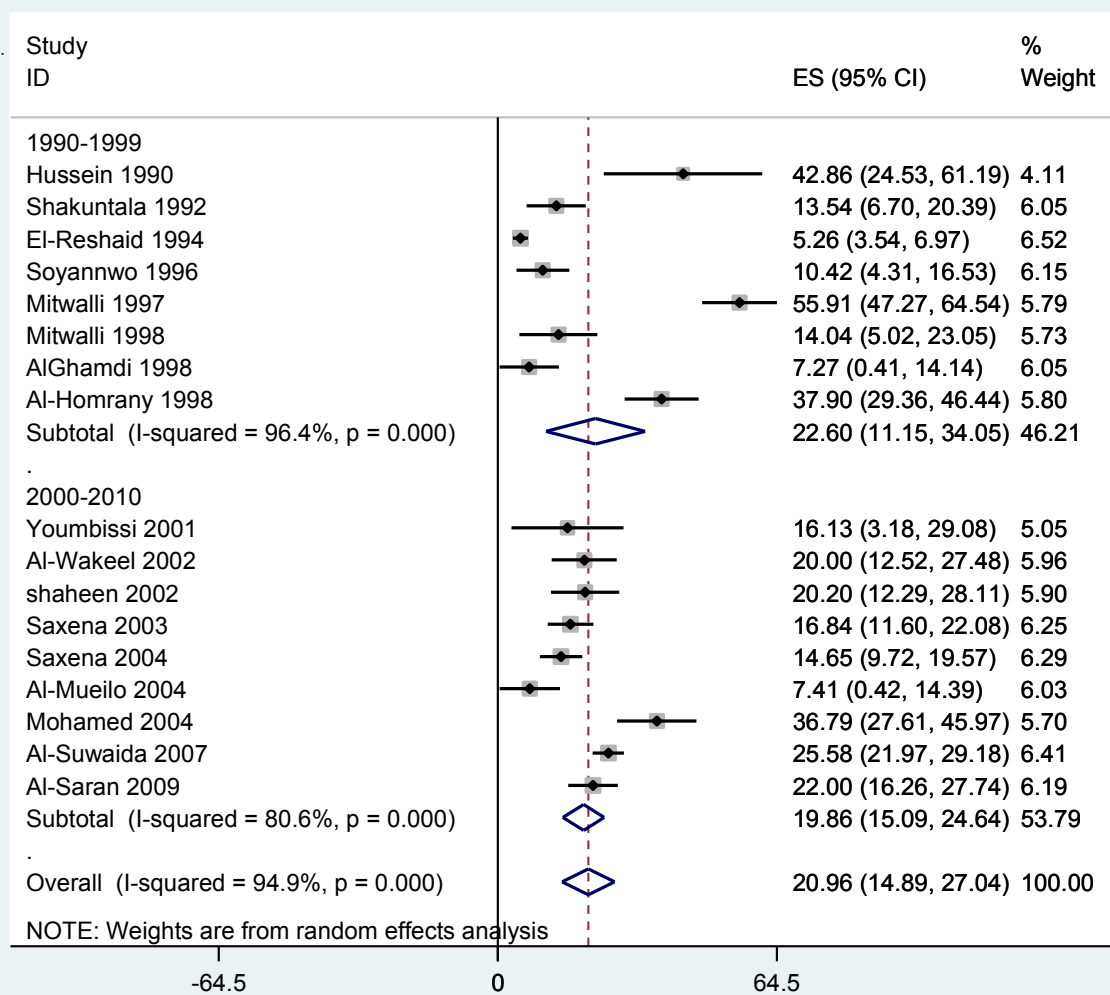


Figure 3.16. Forest plot showing the pooled estimate of the prevalence of uncertain aetiology as a cause of ESRD in the countries of the GCC.

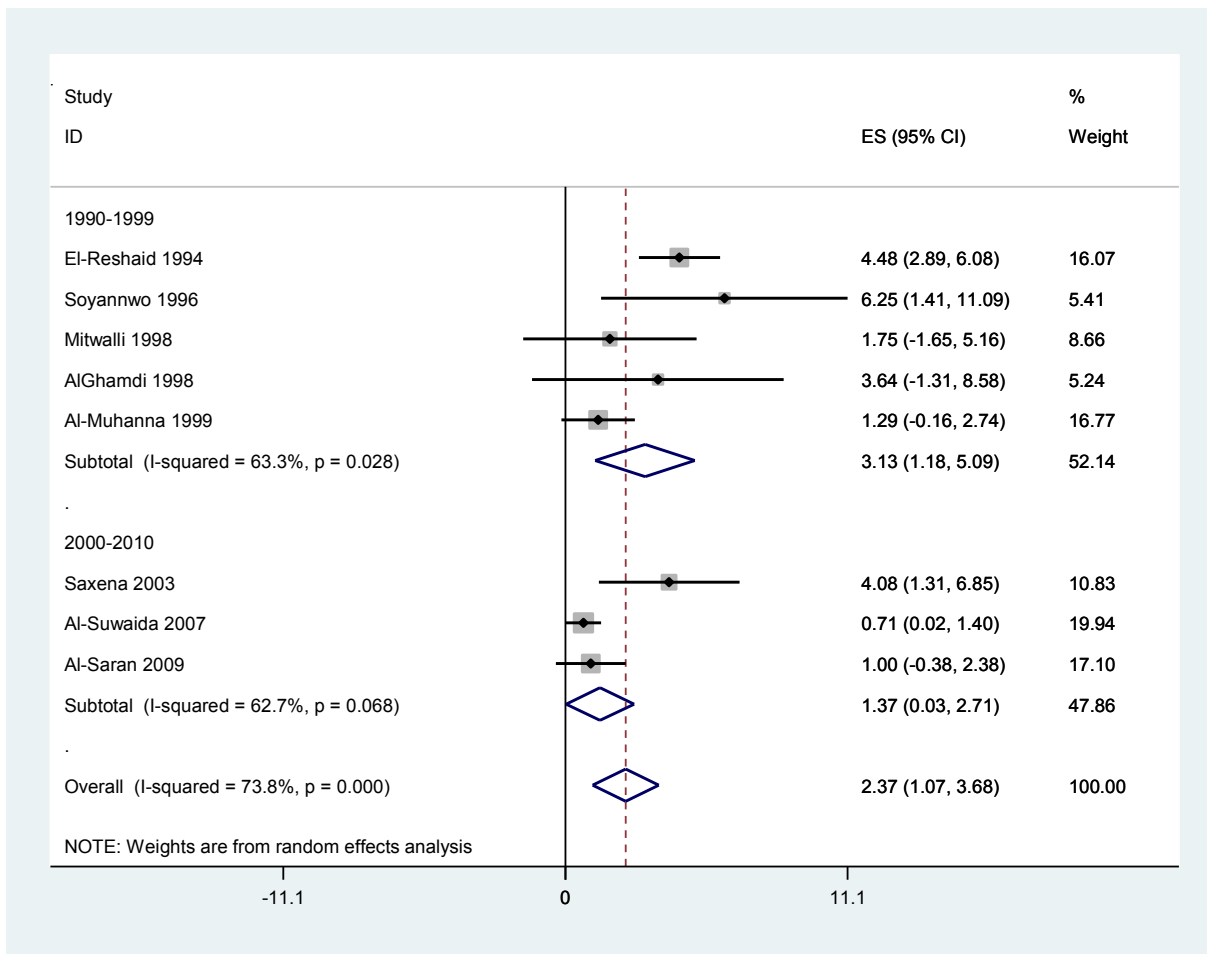


Figure 3.17. Forest plot showing the pooled estimate of the prevalence of other conditions as a cause of ESRD in the countries of the GCC.

Table 3.6. Summary of reported diabetic nephropathy as a cause of ESRD

Ref	Author	Year	Location	Sample size	DN	
					No.	%
(76)	Shakuntala	1992	UAE/Abu Dhabi	96	13	13.5
(77)	El-Reshaid	1994	Kuwait	647	95	14.7
(89)	Mitwalli	1997	KSA/Gizan, Madinah	127	17	13.4
(79)	Al-Suwaida	2007	GCC	563	223	39.6
(88)	Soyannwo	1996	KSA/Centre	96	19	19.8
(94)	Mitwalli	1998	KSA/Centre	57	11	19.3
(92)	AlGhamdi	1998	KSA/Centre	55	11	20.0
(119)	Al-Wakeel	2002	KSA/Centre	110	26	23.6
(117)	Al-Saran	2009	KSA/Centre	200	82	41.0
(95)	Al-Muhanna	1999	KSA/East	233	65	27.9
(103)	Al-Khunaizi	2003	KSA/East	37	22	59.5
(101)	Saxena	2003	KSA/East	196	54	27.6
(107)	Saxena	2004	KSA/East	198	56	28.3
(104)	Al-Mueilo	2004	KSA/East	54	13	24.1
(89)	Mitwalli	1997	KSA/South	82	3	3.7
(93)	Al-Homrany	1998	KSA/South	114	11	9.6
(120)	Khan	2002	KSA/South	67	13	19.4
(80)	Hussein	1990	KSA/West	28	5	17.9
(89)	Mitwalli	1997	KSA/West	45	14	31.1
(99)	Shaheen	2002	KSA/West	99	29	29.3
(105)	Mohamed	2004	KSA/West	106	39	36.8
(110)	Mohamed	2005	KSA/West	125	50	40

DN= diabetic nephropathy

Table 3.7. Summary of reported hypertensive nephropathy as a cause of ESRD

Ref	Author	Year	Location	Sample size	(HT & LV)	
					No.	%
(76)	Shakuntala	1992	UAE/Abu Dhabi	96	9	9.4
(77)	El-Reshaid	1994	Kuwait	647	14	2.2
(89)	Mitwalli	1997	KSA/Gizan, Madinah	127	7	5.5
(79)	Al-Suwaida	2007	GCC	563	43	7.6
(88)	Soyannwo	1996	KSA/Centre	96	47	49
(94)	Mitwalli	1998	KSA/Centre	57	6	10.5
(92)	AlGhamdi	1998	KSA/Centre	55	11	20
(119)	Al-Wakeel	2002	KSA/Centre	110	22	20
(117)	Al-Saran	2009	KSA/Centre	200	40	20
(97)	Youbissi	2001	KSA/East	31	8	25.8
(103)	Al-Khunaizi	2003	KSA/East	37	4	10.8
(104)	Al-Mueilo	2004	KSA/East	54	4	7.4
(89)	Mitwalli	1997	KSA/South	82	3	3.7
(93)	Al-Homrany	1998	KSA/South	114	6	5.3
(80)	Hussein	1990	KSA/West	28	3	10.7
(89)	Mitwalli	1997	KSA/West	45	4	8.9
(99)	Shaheen	2002	KSA/West	99	22	22.2
(105)	Mohamed	2004	KSA/West	106	5	4.7
(110)	Mohamed	2005	KSA/West	94	17	18.1

HT & LV= Hypertension and large vessel disease

Table 3.8. Summary of reported Summary of reported glomerulonephritis as a cause of ESRD

Ref	Author	Year	Location	Sample size	GN	
					No.	%
(76)	Shakuntala	1992	UAE/Abu Dhabi	96	33	34.4
(77)	El-Reshaid	1994	Kuwait	647	155	24.0
(89)	Mitwalli	1997	KSA/Gaizan, Madinah	127	10	7.9
(79)	Al-Suwaida	2007	GCC	563	96	17.1
(88)	Soyannwo	1996	KSA/Centre	96	8	8.3
(94)	Mitwalli	1998	KSA/Centre	57	18	31.6
(92)	Al-Ghamdi	1998	KSA/Centre	55	14	25.5
(119)	Al-Wakeel	2002	KSA/Centre	110	17	15.5
(117)	Al-Saran	2009	KSA/Centre	200	12	6.0
(95)	Al-Muhanna	1999	KSA/East	233	100	42.9
(97)	Youmbissi	2001	KSA/East	31	14	45.2
(103)	Al-Khunaizi	2003	KSA/East	37	3	8.1
(101)	Saxena	2003	KSA/East	196	45	23
(107)	Saxena	2004	KSA/East	198	30	15.2
(104)	Al-Mueilo	2004	KSA/East	54	20	37
(89)	Mitwalli	1997	KSA/South	82	5	6.1
(93)	Al-Homrany	1998	KSA/South	114	38	33.3
(120)	Khan	2002	KSA/South	67	3	4.5
(80)	Hussein	1990	KSA/West	28	4	14.3
(89)	Mitwalli	1997	KSA/West	45	5	11.1
(99)	Shaheen	2002	KSA/West	99	9	9.1
(105)	Mohamed	2004	KSA/West	106	8	7.5
(110)	Mohamed	2005	KSA/West	125	8	6.4

GN= glomerulonephritis

Table 3.9. Summary of reported Summary of reported secondary GN/Vasculitis as causes of ESRD

Ref	Author	Year	Location	Sample size	HUS		SLE	
					No.	%	No.	%
(76)	Shakuntala	1992	UAE/Abu Dhabi	96	–	–	1	1
(77)	El-Reshaid	1994	Kuwait	647	–	–	18	2.8
(88)	Soyannwo	1996	KSA/Centre	96	–	–	2	2.1
(119)	Al-Wakeel	2002	KSA/Centre	110	–	–	11	10
(117)	Al-Saran	2009	KSA/Centre	200	–	–	6	3
(95)	Al-Muhanna	1999	KSA/East	233	3	1.3	10	4.3
(101)	Saxena	2003	KSA/East	196	–	–	18	9.2
(107)	Saxena	2004	KSA/East	198	–	–	18	9.1
(104)	Al-Mueilo	2004	KSA/East	54	–	–	3	5.6
(120)	Khan	2002	KSA/South	67	–	–	3	4.5
(80)	Hussein	1990	KSA/West	28	–	–	1	3.6

HUS= Haemolytic uremic syndrome, SLE= systemic lupus erythematosus

Table 3.10. Summary of reported interstitial nephritis/Pyelonephritis as causes of ESRD

Ref	Author	Year	Location	Sample size	IN		PN		OUP		AN	
					No.	%	No.	%	No.	%	No.	%
(76)	Shakuntala	1992	UAE/Abu Dhabi	96	–	–	18	18.8	–	–	–	–
(77)	El-Reshaid	1994	Kuwait	647	–	–	250	38.6	33	5.1	–	–
(89)	Mitwalli	1997	KSA/Gizan, Madinah	127	4	3.1	5	3.9	8	6.3	–	–
(79)	Al-Suwaida	2007	GCC	563	32	5.7	–	–	–	–	–	–
(88)	Soyannwo	1996	KSA/Centre	96	–	–	5	5.2	12	12.5	–	–
(94)	Mitwalli	1998	KSA/Centre	57	–	–	8	14	1	1.8	1	1.8
(92)	AlGhamdi	1998	KSA/Centre	55	–	–	10	18.2	6	10.9	–	–
(119)	Al-Wakeel	2002	KSA/Centre	110	–	–	12	10.9	–	–	–	–
(117)	Al-Saran	2009	KSA/Centre	200	2	1	–	–	4	2	–	–
(95)	Al-Muhanna	1999	KSA/East	233	13	5.6	–	–	15	6.4	–	–
(97)	Youmbissi	2001	KSA/East	31	–	–	–	–	4	12.9	–	–
(101)	Saxena	2003	KSA/East	196	–	–	18	9.2	3	1.5	4	2
(107)	Saxena	2004	KSA/East	198	–	–	21	10.6	13	6.6	–	–
(104)	Al-Mueilo	2004	KSA/East	54	4	7.4	–	–	–	–	–	–
(89)	Mitwalli	1997	KSA/South	82	2	2.4	5	6.1	6	7.3	–	–
(93)	Al-Homrany	1998	KSA/South	114	–	–	1	0.9	3	2.6	–	–
(120)	Khan	2002	KSA/South	67	–	–	7	10.4	3	4.5	–	–
(80)	Hussein	1990	KSA/West	28	–	–	1	3.6	–	–	–	–
(89)	Mitwalli	1997	KSA/West	45	2	4.4	–	–	2	4.4	–	–
(99)	Shaheen	2002	KSA/West	99	–	–	4	4	7	7.1	–	–
(105)	Mohamed	2004	KSA/West	106	–	–	4	3.8	7	6.6	–	–

IN= Interstitial nephritis or Tubulo-interstitial nephritis, PN= Pyelonephritis, OUP= Obstructive uropathy, AN= Analgesic abuse

Table 3.11. Summary of reported Cystic/Hereditary/Congenital diseases as causes of ESRD

Ref	Study ID	Year	Location	Sample size	Polycystic kidney		Medullary cystic		Congenital/Hereditary	
					No.	%	No.	%	No.	%
(76)	Shakuntala	1992	UAE/Abu Dhabi	96	6	6.3	1	1	1	1
(77)	El-Reshaid	1994	Kuwait	647	19	2.9	—	—	—	—
(89)	Mitwalli	1997	KSA/Gizan, Madinah	127	—	—	—	—	5	3.9
(79)	Al-Suwaida	2007	GCC	563	17	3	—	—	4	0.7
(88)	Soyannwo	1996	KSA/Centre	96	—	—	—	—	23	24
(94)	Mitwalli	1998	KSA/Centre	57	2	3.5	—	—	—	—
(117)	Al-Saran	2009	KSA/Centre	200	—	—	—	—	8	4
(95)	Al-Muhanna	1999	KSA/East	233	—	—	—	—	20	8.6
(101)	Saxena	2003	KSA/East	196	10	5.1	3	1.5	—	—
(107)	Saxena	2004	KSA/East	198	10	5.1	3	1.5	—	—
(104)	Al-Mueilo	2004	KSA/East	54	—	3.7	—	—	2	3.7
(89)	Mitwalli	1997	KSA/South	82	—	—	—	—	5	6.1
(120)	Khan	2002	KSA/South	67	4	6	—	—	4	6
(80)	Hussein	1990	KSA/West	28	—	—	2	7.1	—	—
(89)	Mitwalli	1997	KSA/West	45	—	—	—	—	4	8.9
(99)	Shaheen	2002	KSA/West	99	6	6.1	2	2	—	—
(105)	Mohamed	2004	KSA/West	106	4	3.8	—	—	—	—

Medullary cystic disease= renal calculi or nephrolithiasis, Hereditary disease including Alport's syndrome, Congenital disease= hypoplastic kidney renal hypoplasia or dysplasia

Table 3.12. Summary of reported miscellaneous conditions as causes of ESRD

Ref	Study ID	Year	Location	Sample size	Aetiology uncertain		*Other conditions	
					No.	%	No.	%
(76)	Shakuntala	1992	UAE/Abu Dhabi	96	13	13.5	—	—
(77)	El-Reshaid	1994	Kuwait	647	34	5.3	29	4.5
(89)	Mitwalli	1997	KSA/Gizan, Madinah	127	71	55.9	—	—
(88)	Al-Suwaida	2007	GCC	563	144	25.6	4	0.7
(88)	Soyannwo	1996	KSA/Centre	96	10	10.4	6	6.3
(94)	Mitwalli	1998	KSA/Centre	57	8	14	1	1.8
(92)	AlGhamdi	1998	KSA/Centre	55	4	7.3	2	3.6
(119)	Al-Wakeel	2002	KSA/Centre	110	22	20	—	0
(117)	Al-Saran	2009	KSA/Centre	200	44	22	2	1.0
(95)	Al-Muhanna	1999	KSA/East	233	—	—	3	1.3
(97)	Youmbissi	2001	KSA/East	31	5	16.1	—	—
(101)	Saxena	2003	KSA/East	196	33	16.8	8	4.1
(107)	Saxena	2004	KSA/East	198	29	14.6	—	—
(104)	Al-Mueilo	2004	KSA/East	54	4	7.4	—	—
(93)	Al-Homrany	1998	KSA/South	124	47	37.9	—	—
(89)	Mitwalli	1997	KSA/South	82	57	69.5	—	—
(80)	Hussein	1990	KSA/West	28	12	42.9	—	—
(89)	Mitwalli	1997	KSA/West	45	14	31.1	—	—
(99)	Shaheen	2002	KSA/West	99	20	20.2	—	—
(105)	Mohamed	2004	KSA/West	106	39	36.8	—	—

*Other conditions including rarely reported conditions such as schistosomiasis, tuberculosis, sickle cell nephropathy, contrast nephropathy, multiple myeloma and others.

Co-morbid conditions

Chronic diseases

This group included diabetes, hypertension, defined as an elevation of blood pressure (>160/95 mmHg), cardiovascular disease and vascular disease. Meta-analysis showed that the summarised estimate of diabetes prevalence is 51.26% (95%CI: 44.81%, 57.72%) with an I-square of 69.3% [Figure 2.18]. Hypertension prevalence is 66.67% (95%CI: 49.58%, 83.76%) with high heterogeneity (I-square= 97.4%) [Figure 2.19]. The summarised estimate of cardiovascular disease prevalence is 28.27% (95%CI: 13.71%, 42.83%) with (I-square= 97.2%) [Figure 2.20]. One study reported the prevalence of vascular disease as a co-morbid condition to be 11.7% (95%CI: 9.18%, 14.67%) (79) [Table 2.13].

Infectious disease

This group included HCV, HBV, TB, peritonitis, and nasal carriage of *Staphylococcus aureus*. The most frequently reported and prevalent infectious disease in ESRD patients was HCV, which is more prevalent among haemodialysis patients than peritoneal dialysis patients. The summarised estimate of HCV prevalence is 41.37% (95%CI: 24.54%, 58.21%) with (I-square= 98.4%). The prevalence of HCV has apparently declined from 44.23% (95%CI: 22.12%, 66.33%; I-square= 98.9%) in the period 1990-1999 to 34.87% (95%CI: 18.57%, 51.17%; I-square= 87.2%) in the period 2000-2010 [Figure 2.21]. Three studies were conducted in Saudi Arabia in the period 1990-1999 which reported the prevalence of HBV among ESRD patients, and the summarised estimate was 32.35% (95%CI: 4.33%, 60.38%; I-square= 98.5%) [Figure 2.22]. Five studies reported the prevalence of TB among ESRD patients and were conducted in Saudi Arabia; the summarised prevalence of TB was 14.56% (95%CI: 6.27, 22.85; I-square= 96.3%) [Figure 2.23]. The prevalence of nasal carriage of *Staphylococcus aureus*, which is associated with vascular access related septicaemia, was reported as a co-morbid condition among 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%CI: 31.4%, 45%) (102, 108). The incidence of peritonitis was reported in only one study as 0.62% among continuous ambulatory peritoneal dialysis patients, with a prevalence of 4.69% (95%CI: 2.8%, 7.3%) (97) [Table 2.14].

Other co-morbid conditions and complications

This group included anaemia, bone disease, gastrointestinal abnormalities, liver disease, depression, malnutrition, and restless leg syndrome. Meta-analysis showed that the summarised estimate of liver disease prevalence is 17.96% (95%CI: 8.20%, 27.73%) with an I-square of 93.9% [Figure 2.24]. The prevalence of anaemia, which is defined as haemoglobin <110 g/L or haematocrit <30%, was reported in two studies in this review. One study was conducted in Saudi Arabia in Riyadh City, and reported the prevalence of anaemia as 47.5% (95%CI: 34.59%, 60.73%) (113), while another study reported the prevalence of anaemia for all of the GCC countries to be 33.75% (95%CI: 29.85%, 37.82%) (79). Bone disease, which includes osteosclerosis, osteodystrophy, osteopenia, subperiosteal erosions, bone deformities, soft tissue calcification, and osteomalacia, was reported in only two studies, both of which were conducted in Saudi Arabia and reported the prevalence to be 28.92% (95%CI: 24.05%, 34.18%) in Taief (85) and 70.17% (95%CI: 56.60%, 81.57%) in Riyadh (94). The prevalence of depression was reported in two studies: one study conducted in Saudi Arabia in Abha City reported the prevalence of depression at 59.26% (95%CI: 45.03%, 72.43%) (98), while the other study, conducted in Bahrain, reported the prevalence of depression among men with ESRD as 48%, which is higher than the level reported among women 42% (78). The prevalence of malnutrition was assessed using the subjective global assessment score developed to assess post-operative nutritional state, restless leg, and gastrointestinal abnormalities; these values were reported as 32% (95%CI: 25.60%, 38.95%) (117), 50% (95%CI: 40.49%, 59.51%) (116), and 90.74% (95%CI: 79.70%, 96.92%) (104), respectively [Table 2.15].

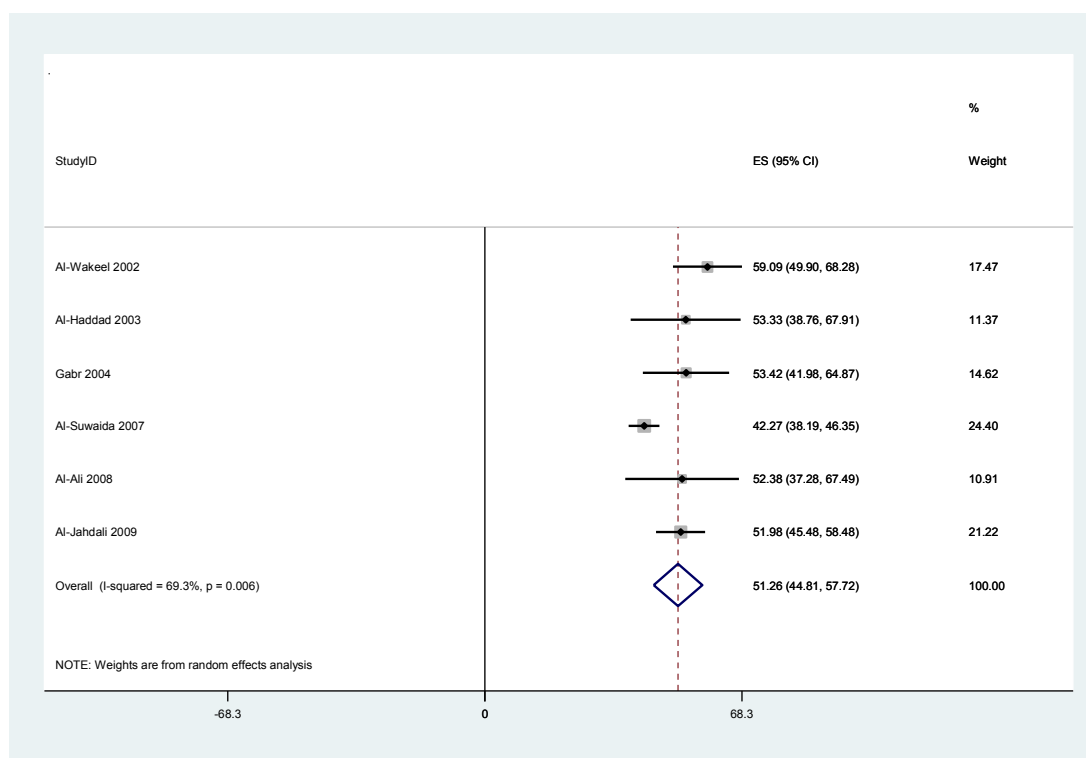


Figure 3.18. Forest plot showing the pooled estimate of the prevalence of diabetes as a co-morbid condition among patients with ESRD in the countries of the GCC.

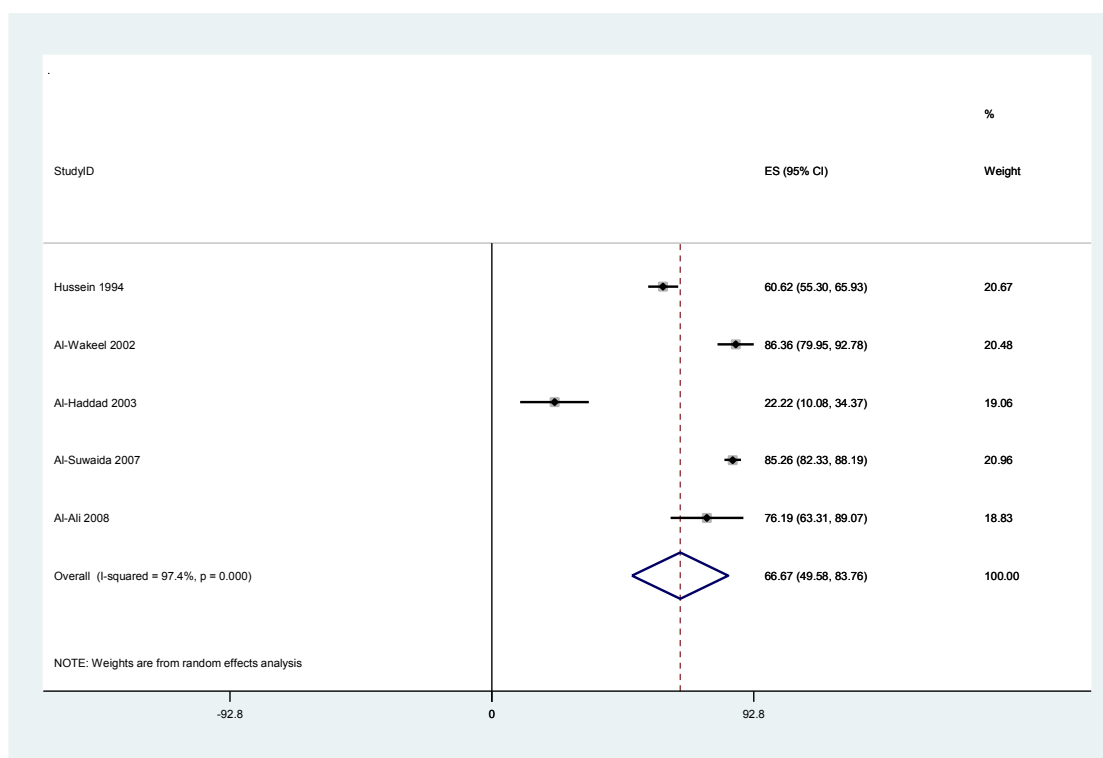


Figure 3.19. Forest plot showing the pooled estimate of the prevalence of hypertension as a co-morbid condition among patients with ESRD in the countries of the GCC.

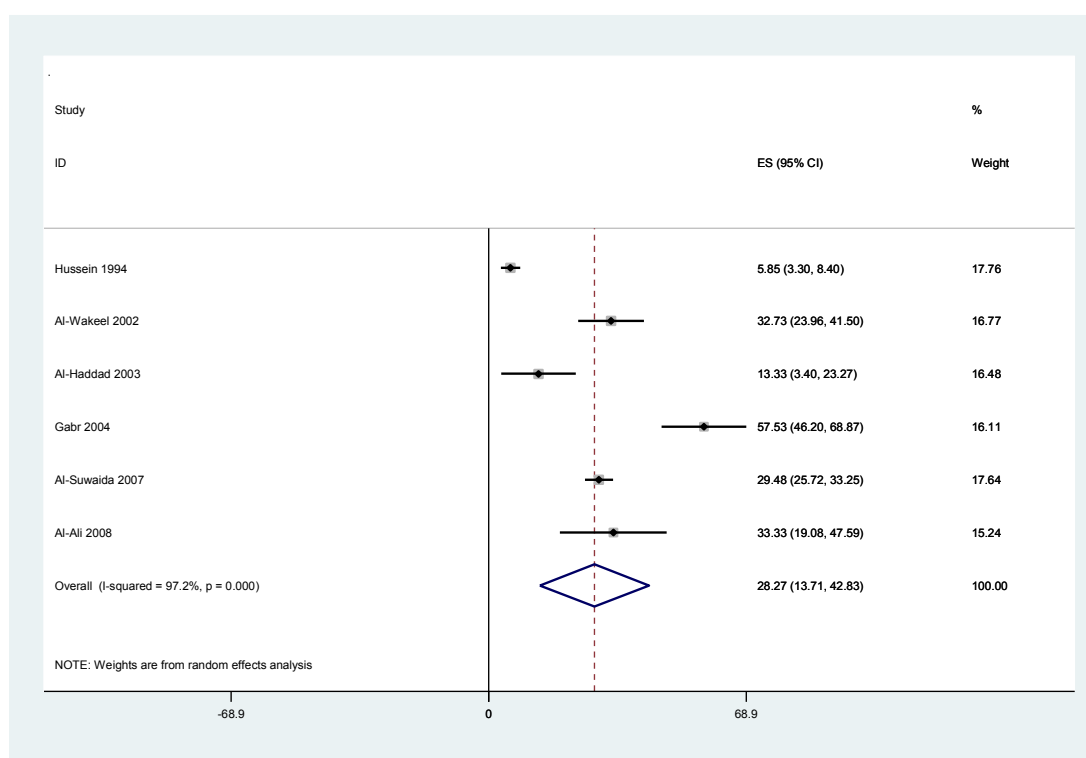


Figure 3.20. Forest plot showing the pooled estimate of the prevalence of cardiovascular diseases as a co-morbid condition among patients with ESRD in the countries of the GCC.

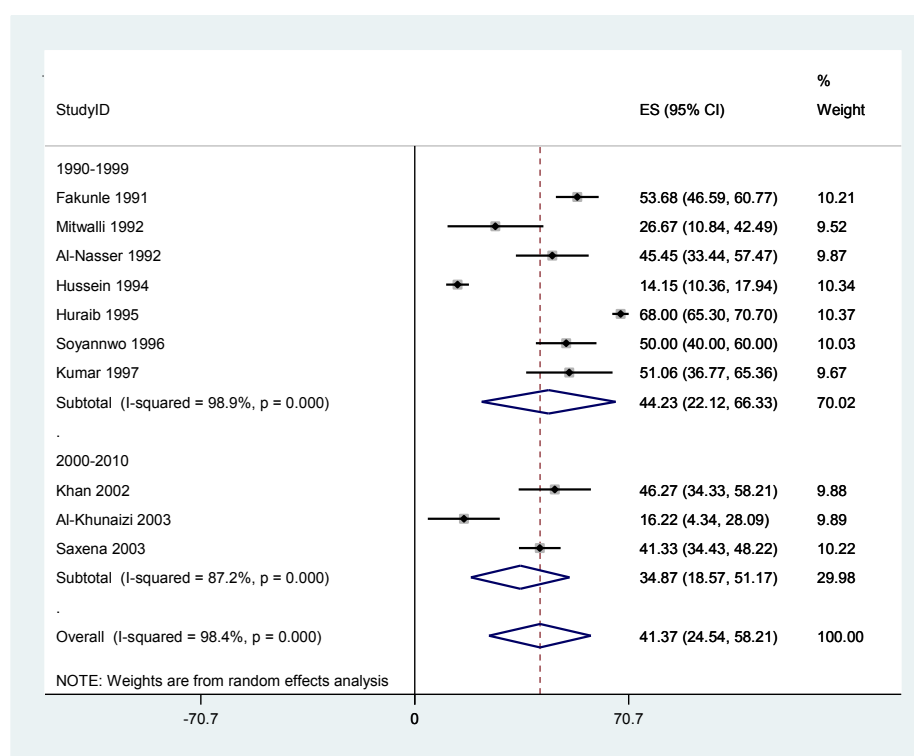


Figure 3.21. Forest plot showing the pooled estimate of the prevalence of HCV as a co-morbid condition among patients with ESRD in the countries of the GCC.

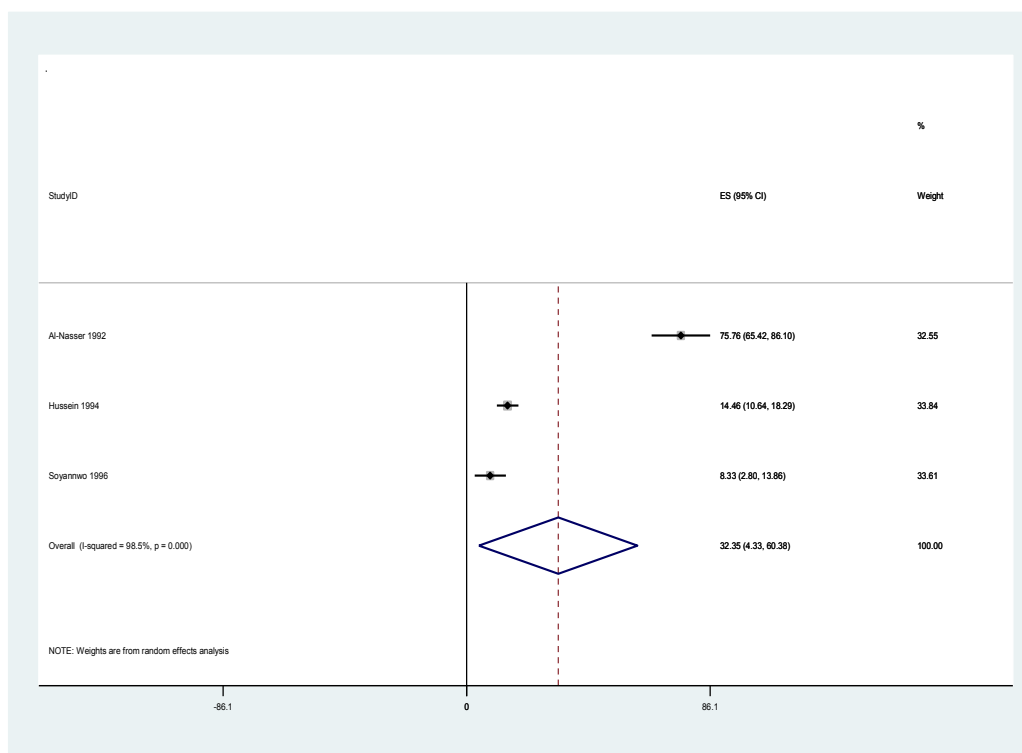


Figure 3.22. Forest plot showing the pooled estimate of the prevalence of HBV as a co-morbid condition among patients with ESRD in the countries of the GCC.

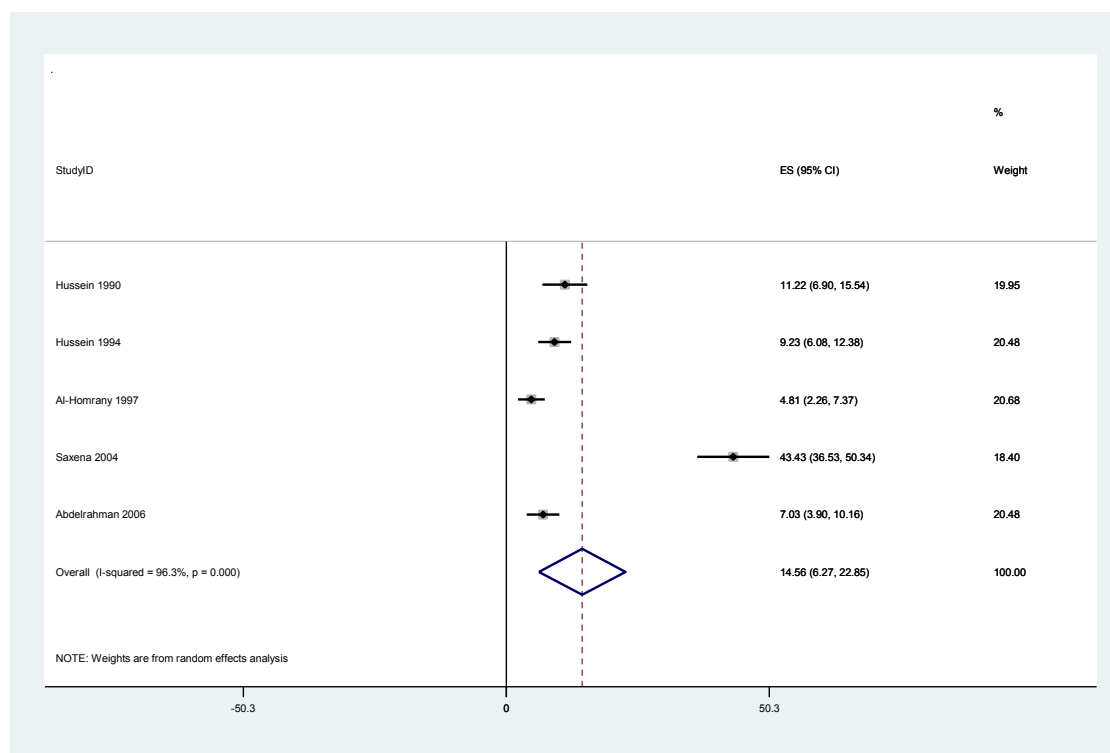


Figure 3.23. Forest plot showing the pooled estimate of the prevalence of TB as a co-morbid condition among patients with ESRD in the countries of the GCC.

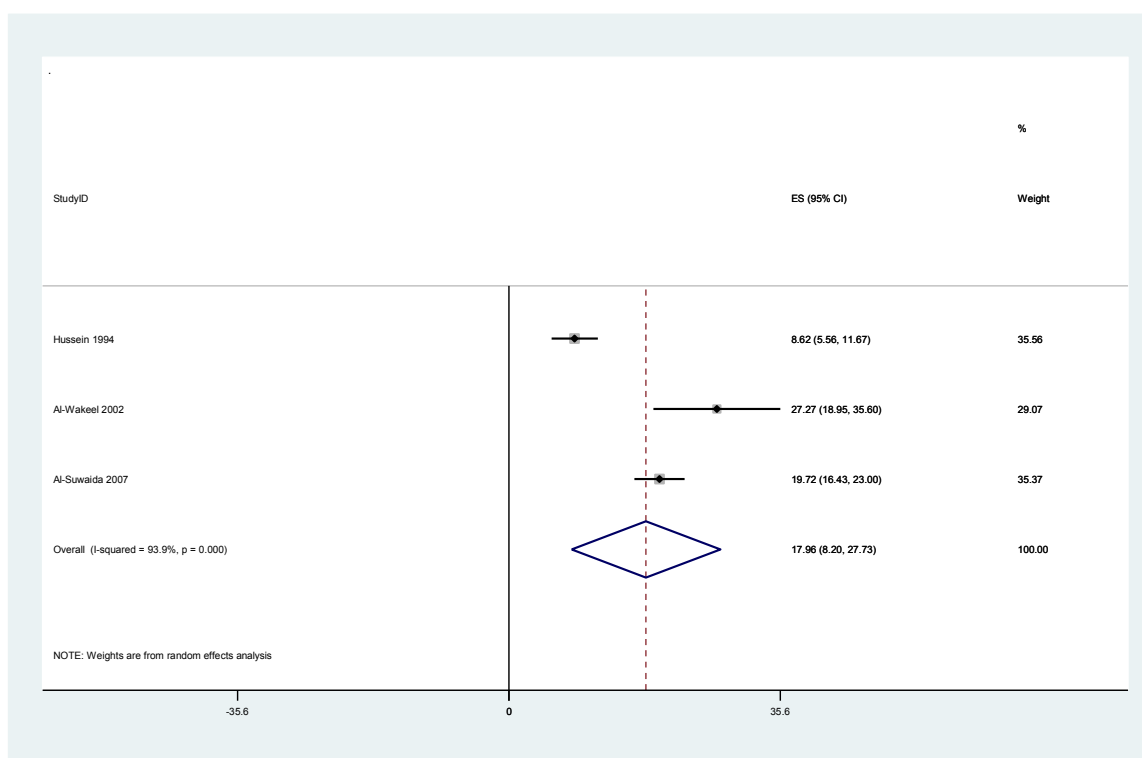


Figure 3.24. Forest plot showing the pooled estimate of the prevalence of liver disease as a co-morbid condition among patients with ESRD in the countries of the GCC.

Table 3.13. Summary of reported chronic disease as co-morbidities in the ESRD population

Ref	Author	Year	Locations	Sample size	CVD		Vascular disease		Hypertension		Diabetes	
					No.	%	No.	%	No.	%	No.	%
(78)	Al-Haddad	2003	Bahrain	45	6	13.3	—	—	10	22.2	24	53.3
(79)	Al-Suwaida	2007	GCC	563	166	29.5	66	11.7	480	85.3	238	42.3
(116)	Al-Jahdali	2009	KSA/Riyadh, Jeddah	227	—	—	—	—	—	—	118	52
(85)	Hussein	1994	KSA/West	325	19	5.8	—	—	197	60.6	—	—
(119)	Al-Wakeel	2002	KSA/Centre	110	36	32.7	—	—	95	86.4	65	59.1
(109)	Gabr	2004	KSA/Centre	73	42	57.5	—	—	—	—	39	53.4
(114)	Al-Ali	2008	KSA/East	42	14	33.3	—	—	32	76.2	22	52.4

CVD= Cardiovascular diseases

Table 3.14. Summary of reported infectious diseases as co-morbid conditions

Ref	Author	Year	Location	Sample size	TB		Peritonitis		NCOSA		HCV		HBV	
					No.	%	No.	%	No.	%	No.	%	No.	%
(87)	Huraib	1995	KSA	1147	–	–	–	–	–	–	780	68	–	–
(82)	Fakunle	1991	KSA/ Centre	190	–	–	–	–	–	–	102	53.7	–	–
(84)	Mitwalli	1992	KSA/ Centre	30	–	–	–	–	–	–	8	26.7	–	–
(88)	Soyannwo	1996	KSA/ Centre	96	–	–	–	–	–	–	48	50	8	8.3
(97)	Youmbissi	2001	KSA/East	384	–	–	18	4.7	–	–	–	–	–	–
(103)	Al-Khunaizi	2003	KSA/East	37	–	–	–	–	–	–	6	16.2	–	–
(101)	Saxena	2003	KSA/East	196	–	–	–	–	–	–	81	41.3	–	–
(102)	Saxena	2003	KSA/East	208	–	–	–	–	79	38	–	–	–	–
(108)	Saxena	2004	KSA/East	205	–	–	–	–	78	38	–	–	–	–
(107)	Saxena	2004	KSA/East	198	86	43.4	–	–	–	–	–	–	–	–
(111)	Abdelrahman	2006	KSA/East	256	18	7	–	–	–	–	–	–	–	–
(83)	Al-Nasser	1992	KSA/South	66	–	–	–	–	–	–	30	45.5	50	75.8
(90)	Al-Homrany	1997	KSA/South	270	13	4.8	–	–	–	–	–	–	–	–
(91)	Kumar	1997	KSA/South	47	–	–	–	–	–	–	24	51.1	–	–
(120)	Khan	2002	KSA/South	67	–	–	–	–	–	–	31	46.3	–	–
(80)	Hussein	1990	KSA/West	205	23	11.2	–	–	–	–	–	–	–	–
(85)	Hussein	1994	KSA/West	325	30	9.2	–	–	–	–	46	14.2	47	14.5

TB= Tuberculosis, NCOSA= Nasal carriage of Staphylococcus aureus, HCV= Hepatitis C Virus, HBV= Hepatitis B

Table 3.15. Summary of reported other co-morbid conditions in the ESRD population

Ref	Author	Year	Location	Sample size	Bone disease		Depression		Anaemia		GIA		RLS		MN		Liver disease	
					No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
(78)	Al-Haddad	2003	Bahrain	45	–	–	21	46.7	–	–	–	–	–	–	–	–	–	–
(79)	Al-Suwaida	2007	GCC	563	–	–	–	–	190	33.7	–	–	–	–	–	–	111	19.7
(116)	Al-Jahdali	2009	KSA/Riyadh, Jeddah	114	–	–	–	–	–	–	–	–	57	50	–	–	–	–
(104)	Al-Mueilo	2004	KSA/East	54	–	–	–	–	–	–	49	90.7	–	–	–	–	–	–
(85)	Hussein	1994	KSA/West	325	94	28.9	–	–	–	–	–	–	–	–	–	–	28	8.6
(98)	Al-Homrany	2001	KSA/South	54	–	–	32	59.3	–	–	–	–	–	–	–	–	–	–
(94)	Mitwalli	1998	KSA/Centre	57	40	70.2	–	–	–	–	–	–	–	–	–	–	–	–
(119)	Al-Wakeel	2002	KSA/Centre	110	–	–	–	–	–	–	–	–	–	–	–	–	30	27.3
(113)	Al-Shatwi	2007	KSA/Centre	61	–	–	–	–	29	47.5	–	–	–	–	–	–	–	–
(117)	Al-Saran	2009	KSA/Centre	200	–	–	–	–	–	–	–	–	–	–	64	32	–	–

GIA= Gastrointestinal abnormalities, RLS= Restless leg syndrome, MN= malnutrition

Causes of mortality in ESRD patients

Causes such as pulmonary oedema, ischemic heart disease, and myocardial infarction were grouped under one category, cardiovascular disease. Meta-analysis showed that the summarised estimate of cardiovascular disease is 44.76% (95%CI: 25.21%, 64.32%) with an I-square of 93.2% [Figure 2.25], while cerebrovascular disease is 11.64% (95%CI: 1.48%, 21.80%) with an I-square of 83.5% [Figure 2.26]. The summarised estimate of sepsis as a cause of death in ESRD patients is 19.61% (95%CI: 12.60%, 26.62%) with an I-square of 35.8% [Figure 2.26]. Malfunction of dialysis access was only reported in one study as a cause of death in ESRD patients at 32.43% (95%CI: 18.01%, 49.78%) (103). Pulmonary disease as a cause of death was reported in two studies; one reported the percentage of pulmonary disease as a cause of death at 4.35% (95%CI: 0.56%, 14.84%) (85), and the other reported the percentage as 9.43% (95%CI: 3.13%, 20.66%) (95). Gastrointestinal bleeding was reported as a cause of death in two studies as 4.3% (95%CI: 0.53%, 14.84%) (85), and 10.81% (95%CI: 3.02%, 25.42%) (103) [Table 2.16].

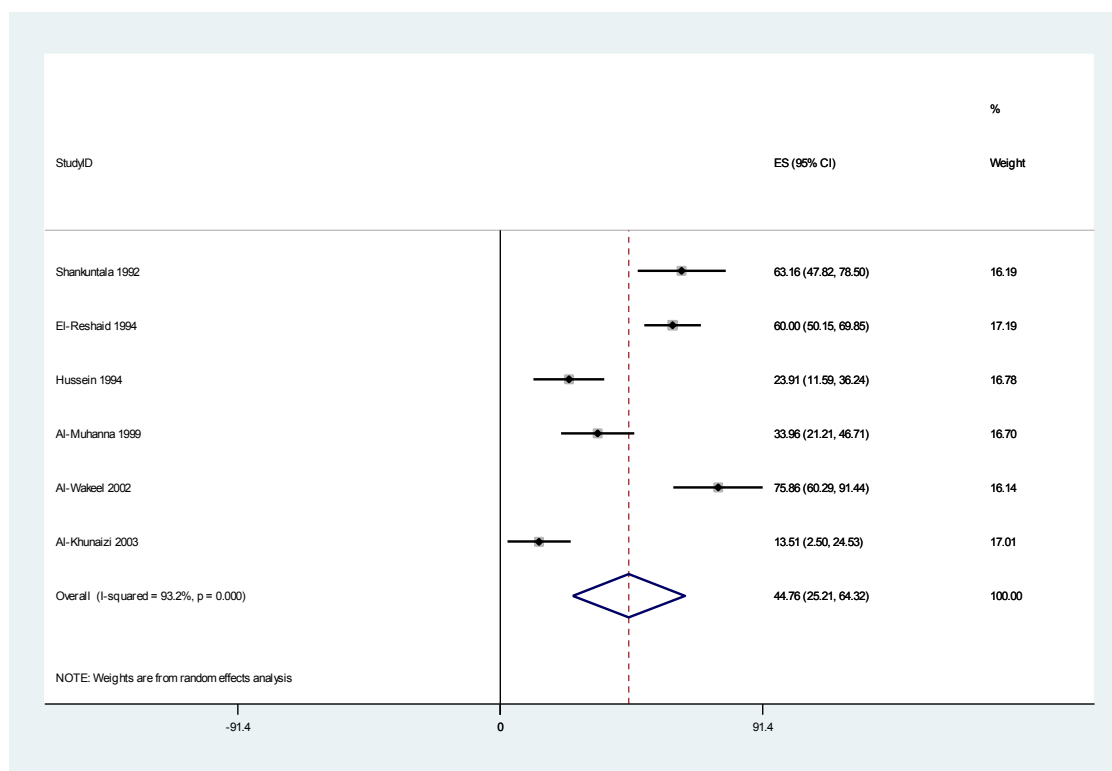


Figure 3.25. Forest plot showing the pooled estimate of the prevalence of cardiovascular disease as a cause of death among patients with ESRD in the countries of the GCC.

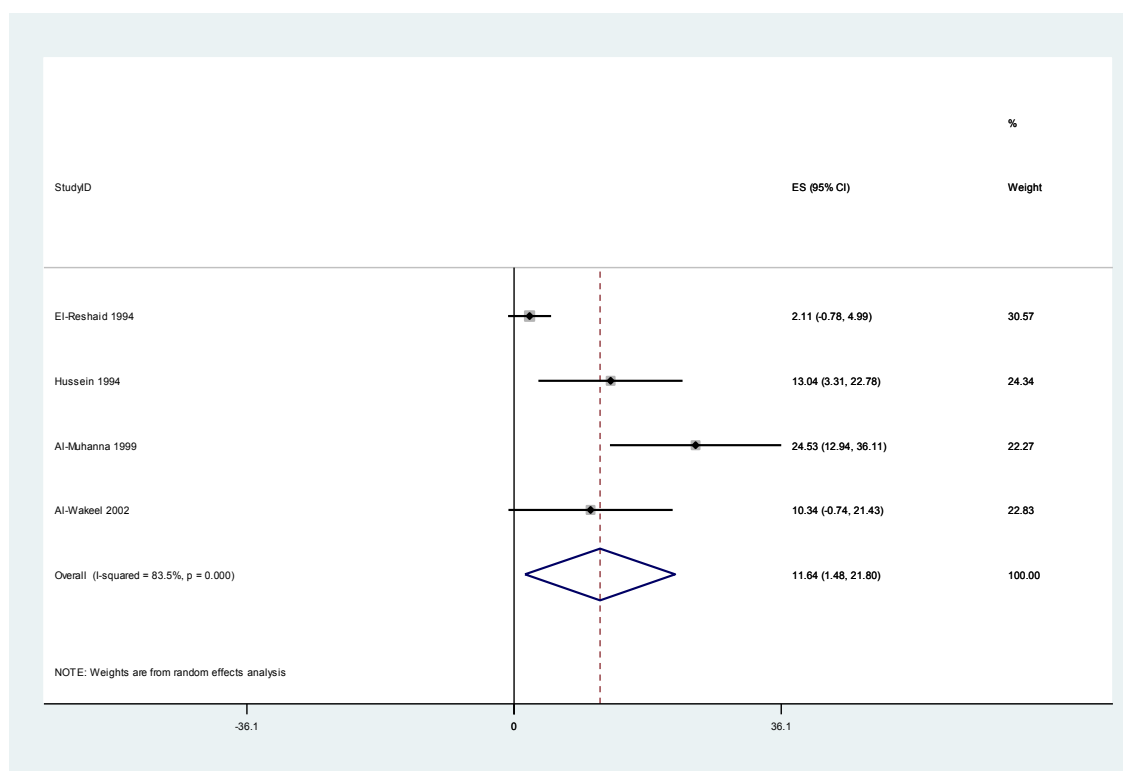


Figure 3.26. Forest plot showing the pooled estimate of the prevalence of cerebrovascular disease as a cause of death among patients with ESRD in the countries of the GCC.

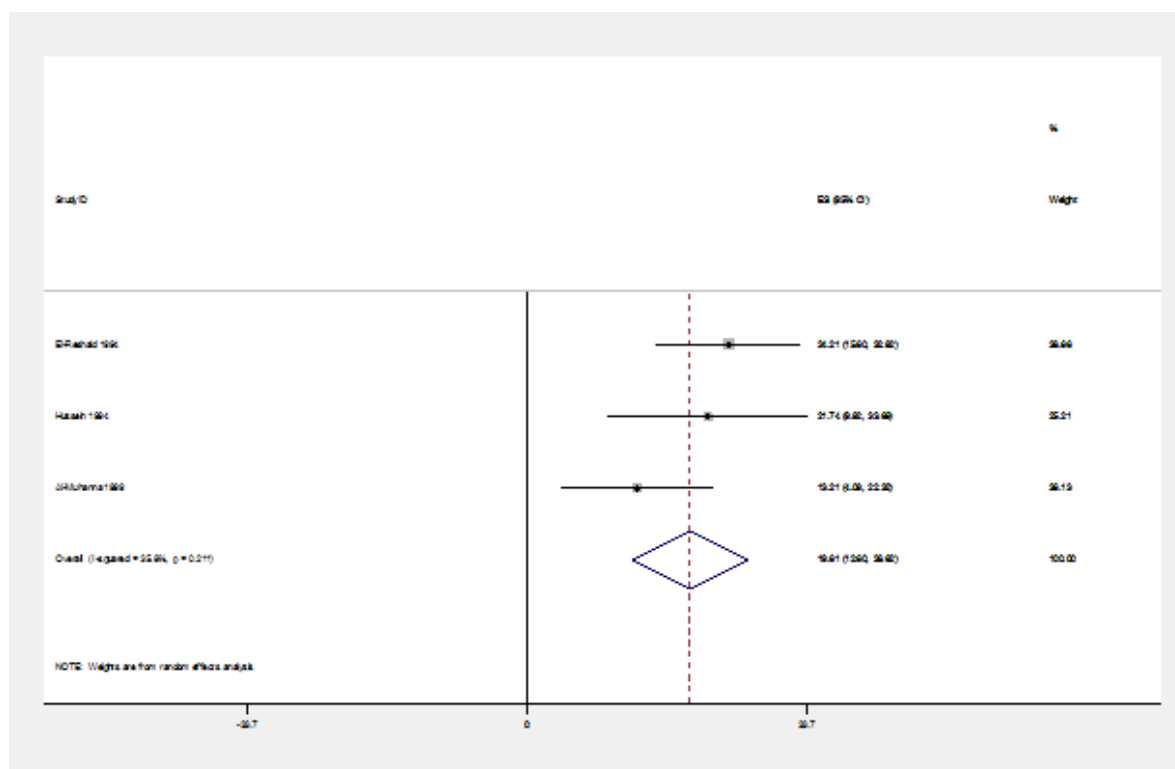


Figure 3.27. Forest plot showing the pooled estimate of the prevalence of sepsis as a cause of death among patients with ESRD in the countries of the GCC.

Table 3.16. Summary of reported mortality causes among ESRD patients

Ref	Author	Year	Location	Sample size	CVD		CVA		Sepsis		PI		PE		GIB		MLG		MODA		Miscellaneous	
					No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
(76)	Shankuntala	1992	UAE/Abu Dhabi	38	24	63	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
(77)	El-Reshaid	1994	Kuwait	95	57	60	2	2	23	24.2	–	–	–	–	–	–	–	–	–	–	10	11
(119)	Al-Wakeel	2002	KSA/Centre	29	22	76	3	10	–	–	–	–	–	–	–	–	–	–	–	–	–	–
(95)	Al-Muhanna	1999	KSA/East	53	18	34	13	25	7	29	3	6	2	4	–	–	5	9	–	–	5	9
(103)	Al-Khunaizi	2003	KSA/East	37	5	14	–	–	–	–	–	–	–	–	4	11	–	–	12	32	–	–
(85)	Hussein	1994	KSA/West	46	11	24	6	13	10	77	–	–	2	4	2	4	–	–	–	–	15	33

CVD= Cardiovascular disease, CVA= Cerebrovascular accident, PI= Pulmonary infection, PE=Pulmonary embolism, GIB= Gastrointestinal Bleeding, MLG= Malignancy, MODA=Malfunction of dialysis access, Miscellaneous= road traffic accident, refused treatment, cardiac arrest, and unknown cause

Discussion

This review gives an overview of the epidemiological pattern of ESRD in the countries of the GCC. The demographic distribution of ESRD patients in the countries of the GCC shows that the overall proportion of males (52%) with ESRD is slightly higher than females (48%), and that the age group with the highest prevalence is between 41 and 53 years old. This is because the prevalence of risk factors for ESRD among males is higher than females in the general populations in the world as in Saudi Arabia(121-123), which is where most of the included studies were conducted, while the middle-aged group constitutes the majority of the population, and elderly people (those aged >65) constitute only 3% (46). This clarifies why the proportion of elderly patients with ESRD was small in the studies included in this review. This finding is similar to the demographic distribution for dialysis population in Saudi Arabia that was reported by SCOT in 2011 (60). The most frequent type of RRT in the GCC countries is dialysis, particularly haemodialysis, which might be due to the low rate of renal transplantation or to insufficient organ donation to meet demand. Renal transplantation prevalence was reported in only five studies and ranged from 3.7% to 47.9% (76, 77, 85, 96, 119). While the SCOT 2011 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 markedly increasing since 1979 in Saudi Arabia (60).

The incidence, prevalence and mortality rate of ESRD in the GCC were not reported sufficiently in studies included in this review. All of the included studies reported the cumulative incidence rate, which does not show changes in the trend; the exception was one study that reported the mean annual growth rate in Gizan of 7.44% in the period from 1987 until 2000 (96). However, two studies in this review that were conducted in Saudi Arabia in Al-Madinah city show that the incidence had increased two-fold from 1988 to 2001 (86, 105); this implies that the incidence has been increasing gradually over time. Furthermore, the mortality rate among ESRD patients in this review varied widely between studies across the region that may relate to differing treatment practices between healthcare centres, which contribute to the variation in outcomes. In addition, it was difficult to track the trend of prevalence and mortality in this review because of gaps in the available data. However, SCOT data show that the mean annual growth rate of dialysis patients is around 8% (60), 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 population growth rate and the rapid socioeconomic development in these countries in recent decades, which has resulted in changing lifestyle and nutrition habits (50). This in turn, plays a role in changing the trend of the prevalence of non-communicable disease such as diabetes, which is the leading global cause of ESRD (42, 124). Many reports have shown evidence of increasing prevalence of the most common causes of ESRD in the GCC such as obesity, hypertension, and diabetes, where the prevalence of diabetes and hypertension is significantly higher in urban populations than rural populations (26, 121, 125). This supports the finding in this review that the prevalence of diabetic nephropathy and hypertensive nephropathy as a cause of ESRD tend to be higher in urban areas than rural areas.

The findings in this review show that the leading cause of ESRD in the GCC was diabetic nephropathy (21%-31%), followed by GN (14%-23%) and hypertensive nephropathy (9%-19%). The prevalence of diabetic nephropathy has been increasing significantly over time, while the prevalence of GN has been decreasing over time. Furthermore, among all of the reported co-morbid conditions in this review, hypertension was the most prevalent chronic condition among patients with ESRD in the countries of the GCC, and ranged between 50% and 84%. In addition, infectious diseases were also prevalent co-morbid conditions, of which HCV infection, which is associated with a high rate of chronic liver disease and cirrhosis (126), was the most prevalent among patients with ESRD in the countries of the GCC, particularly among haemodialysis patients, with a range from 24%-58%. This might be due to many factors, such as the effect of nurse understaffing, which means that the staff were not highly trained overall (106, 127-129). Other factors may increase the risk of HCV, such as the length of dialysis, or the number of blood transfusions that might have involved incomplete or absent anti-HCV screening of donated blood (130); also, diabetic patients and males are more likely to develop HCV (107-109, 127, 131-133). However, this review found that the prevalence of HCV has declined in recent decades, which is a similar finding to that reported in the SCOT report in 2011 (60).

Causes of mortality and hospitalisation among ESRD patients usually result from infectious diseases or complications of dialysis or chronic illness, as they may reflect the quality of

healthcare services or the severity of the chronic illness. The most frequent causes of death in ESRD populations in this review were cardiovascular disease (between 25% and 64% of deaths) and sepsis (13%-27%). Two of the studies included in this review reported the causes of hospitalisation. One study reported that the major cause of hospitalisation was cardiovascular disease followed by vascular access-related problems, while ischemic heart disease contributed to 19% of the total hospitalisation (119). Another study reported the main cause of hospitalisation as vascular access-related problems (34%) (110). However, one of the studies included in this review suggested that the optimisation of arteriovenous fistula (AVF) placement might be a preventative approach to reduce infections associated with vascular access problems among haemodialysis patients, such as *Staphylococcus aureus* infection, which can lead to septicaemia (102). 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 of permanent vascular access for HD patients, and is related to an improved quality of life and increased life expectancy in HD patients (134).

Limitations

This review includes gaps in the data that did not allow tracking the trends of the prevalence and incidence rate of ESRD and mortality rates among patients with ESRD. Furthermore, the majority of studies included in this review were concerned with the haemodialysis population, while there is no available data on either pre-emptive renal transplantation or elderly people receiving supportive care. In addition, this review is prone to 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 have resulted in the exclusion patients with ESRD who did not survive for more than three months. Also, many of included studies did not report the relevant outcomes as primary outcomes. 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 updated estimates for each related outcome, and the majority of studies were given a low score in methodological quality assessment; this might have been because they were not well reported or lacked sufficient data. In addition, the heterogeneity between the studies, which was represented by the I-square value, was high in many estimates for relevant outcomes in this review. Therefore, the lack of a comprehensive national renal registry data or health information system in the countries of the GCC is a critical issue. These data aim to provide a

reliable and up to date source of health information to allow regular assessment for healthcare services. Sufficient information is supposed to be recorded for each ESRD patient, such as demographic and clinical characteristics, RRT, vascular access, primary causes of ESRD, co-morbid conditions, laboratory tests, medications, hospitalisation, death event and cause of death. Each outcome must be recorded and dated by healthcare specialists according to standardised policies, especially in diagnostic procedures, as this review showed that between 15% and 27% of the aetiology of renal disease was uncertain or unknown.

Strengths

This review included all of the epidemiological studies conducted in the GCC up until 2010 and presents adequate and comprehensive information based on epidemiological studies for multiple outcomes related to ESRD. It provides an evidence-based health policy of increasing the burden of ESRD, which helps public health planners and administrators to enable the prediction of healthcare trends and to allocate healthcare resources. Also, this review defines people at high-risk of developing ESRD in the countries of the GCC, namely those of middle age, who are diabetic or hypertensive. This emphasises the importance of developing preventative strategies such as regular screening for people at high risk to detect and manage CKD in the early stages, and to prevent or slow down its progression to ESRD. Those programs may be more cost effective in the future as they increase the early detection of CKD that may attribute to decrease the incidence of ESRD and the number of patients who need RRT (42, 135, 136). Furthermore, this review records all co-morbid conditions and causes of death in ESRD patients in the GCC. This information is extremely valuable for policy makers to assess the current situation and to improve the quality of healthcare management in the countries of the GCC, whereas the quality of healthcare practice should be a target for healthcare providers, in order to improve the quality of life and life expectancy for patients with ESRD. Also, this review provides insight regarding the sources and quality of the current health information system in the GCC, and identifies priority areas for further healthcare management research.

Comparisons

By comparing this review with a similar publication that was undertaken for the countries of the Middle East which the countries of the GCC are a part of, it can be seen that both highlighted

that the incidence of ESRD is increasing substantially, and that diabetes is a dominant cause of ESRD (137). These findings are similar to those reported in the United States and Europe, where diabetes was found to be the predominant cause of ESRD (138-140). This review shows that the prevalence of diabetic nephropathy as a cause of ESRD in the countries of the GCC in the period 2000-2010 was around 33%, which is higher than the reported prevalence of diabetic nephropathy in 2010 in the United Kingdom (26%), but lower than in the United States (54.5%) (141). This review indicates that hypertension is the commonest co-morbid condition in the ESRD population in the countries of the GCC, as outlined in the SCOT report (60); both reports are similar to that which was found in the countries that participate in Dialysis Outcomes and Practice Patterns Study Programs (DOPPS) (141). Furthermore, in comparing the findings of this review with the SCOT report, we found that the prevalence of HCV among ESRD patients in the countries of the GCC to be high: around 35% in the period between 2000-2010 in this review and 26% in the SCOT report in 2011; these results are higher than those reported in Europe (12%) and the United States (7%) (52, 142). The observed variation in outcomes between countries or healthcare centres suggests opportunities for improving healthcare management.

Conclusion

This review presents an evidence-based health policy of the increasing burden of ESRD in the countries of the GCC. This stressed the needs and the importance of preventative strategies for leading causes of ESRD, as this review explored the major causes of ESRD in these countries and the most frequent co-morbid conditions and causes of mortality among patients with ESRD. Accordingly, this review suggested that the dominant cause of ESRD in the GCC was diabetic nephropathy, that the most frequent co-morbid conditions were hypertension and HCV, and that the primary causes of mortality were cardiovascular disease and sepsis. These results identified priority areas for further researches to assess the quality of healthcare management consistently and provide an updated evidence-based health policy, which will help healthcare providers to choose the best intervention that will help to improve healthcare practice outcomes. Furthermore, this review highlights the need for health information systems to allow regular screening for those people at high risk and detect CKD in the early stages, to describe the epidemiological pattern of ESRD in the countries of the GCC, and to conduct further research for assessing the overall quality of healthcare management for patients with ESRD in the countries of the GCC.

CHAPTER 4

Review of pre-end-stage renal disease care in the western region in Saudi Arabia

Abstract

Background

Chronic kidney disease (CKD) has emerged as an important public health issue worldwide, as undiagnosed or late detection cases of CKD are associated with an increased incidence rate and burden of end-stage renal disease (ESRD). The risk factors for CKD have been increasing in the Saudi population. Consequently, the incidence of ESRD has increased substantially over the past three decades with very limited literature on the assessment of pre-ESRD nephrology care practices in Saudi Arabia.

Aims

To assess pre-ESRD care practices in Saudi Arabia by describing the preliminary indicators including: reason for referral to nephrology care, source of referral to nephrology care, duration of pre-ESRD care, and vascular access at the first dialysis; and primary causes of ESRD. Also, to investigate the potential factors that may be associated with late referral to nephrology care practices and its consequences.

Methods

A cross-sectional study was conducted in Al-Noor Kidney Centre and Jeddah Kidney Centre in the western region of Saudi Arabia. Participants were patients with ESRD on haemodialysis during 2011; all requested data were retrieved from medical records retrospectively.

Results

Preliminary indicators of pre-ESRD care showed that a large proportion (47.6% (95%CI: 41.7%, 53.5%)) of haemodialysis patients had not received pre-ESRD nephrology care; 50.6% (95%CI, 45.6%, 55.6%) of patient referrals arrived from the emergency department and the predominant vascular access point for haemodialysis was initially a catheter in 88.3% (95%CI: 84.5%, 91.3%) of patients. Endocrine, nutritional and metabolic diseases, and immune disorders were the principal reason for patient referral, occurring in 50.6% (95%CI: 45.1%, 56.1%) of patients, followed by diseases of the circulatory system in 39.9% (95%CI: 34.6%, 45.3%) of patients. The dominant causes of ESRD in the study sample were hypertensive nephropathy (55.8% (95%CI: 50.8%, 60.7%)) and diabetic nephropathy (24.6% (95%CI: 20.4%, 29.1%)). Factors significantly associated with late referral to nephrology care practices were referral source (p-value<0.0001), reason for referral (p-value=0.005), and vascular access used at first dialysis (p-value<0.0001). Thus, the possibility of initiating haemodialysis with arterio-venous fistula (AVF) increased by 1% (95%CI: 1.00%, 1.02%; p-value=0.02) with each one month increase in pre-ESRD care; while patients who were referred from outpatient clinics were more likely to initiate haemodialysis with AVF compared with those who were referred from an emergency department (OR=3.99; 95%CI: 1.44, 11.02; p-value=0.008). Patients who were referred to nephrology care because of diseases of the circulatory system, as well as endocrine, nutritional and metabolic diseases, and immune disorders, were less likely to initiate haemodialysis with AVF compared with those who were referred because of diseases of the genitourinary system; (OR=0.19; 95%CI: 0.04, 0.89; p-value=0.03), (OR=0.11; 95%CI: 0.02, 0.51; p-value=0.005) respectively.

Conclusion

This study provides evidence to support the need for improving the rate of referring patients with CKD at earlier stages to nephrology care in Saudi Arabia. Potential strategies could involve regular screening of high risk people, encouraging communication between healthcare practitioners, and education on the need to refer patients with CKD to nephrology care at earlier disease stages, and increasing patients' awareness about their health conditions and the potential consequences of their kidney disease.

Background

Chronic kidney disease (CKD) has emerged as an important public health issue worldwide, as undiagnosed or late detection cases of CKD are associated with an increased incidence and prevalence rate of end-stage renal disease (ESRD), and poor outcomes after initiating renal replacement therapy (RRT) (143-146). This increases the need for multidisciplinary management including financial and social support, and medical care (147). Pre-ESRD nephrology care, which is known as early referral of patients with CKD to specialised renal services, can help to preserve renal function and delay the progression of renal failure by preventing and managing the modifiable risk factors associated with CKD and treating secondary complications (35, 148) that including metabolic syndromes (149-151), and anaemia (152-155).

Many studies have shown that a long duration of pre-ESRD nephrology care, which is the period between the first time the patient has been seen by a nephrologist and the first dialysis (148), has a significant effect on the quality of life and survival rate in patients with ESRD before and after initiating RRT (35, 145, 156-158). Improved detection of patients with CKD in its early stages can significantly reduce the risk of cardiovascular morbidity and its consequences such as hospitalisation and death (159-162). Besides, pre-ESRD nephrology care gives an adequate time to prepare patients for RRT, especially those patients who need to create vascular access for dialysis, as maturation of the arterio-venous fistula (AVF) takes from six to eight weeks, and helps to improve pre-emptive renal transplantation treatment which is required for at least one year in preparation (144, 148). The National Kidney Foundation - Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) guidelines recommend that preparation for RRT should start in CKD stage 4, when the estimated glomerular filtration rate (eGFR) is $<30\text{mL/min/1.73m}^2$ (148). This gives time to choose and create a suitable dialysis access point, considering AVF as a modifiable risk factor for bacteraemia and mortality (163, 164), and avoids the need for a catheter as a temporary vascular access. These healthcare practices have a significant impact on improving the prognosis and quality of life among the dialysis population, (164-166) and reducing hospital utilisation and the costs of healthcare (167-170).

In Saudi Arabia, the incidence and prevalence rate of RRT have increased substantially over the last three decades (60). Many reports have shown evidence for an increase in the

prevalence of the most common risk factors for CKD such as obesity associated chronic diseases (26, 49, 50), and metabolic disorders; this in turn increases the risk of developing cardiovascular diseases and diabetes (171, 172). Diabetic nephropathy is the leading cause of ESRD in Saudi Arabia (27, 60, 173). There is limited literature available for assessing the quality of pre-ESRD nephrology care in Saudi Arabia. Only two studies have been conducted to review pre-ESRD nephrology care based on a single centre experience in two different regions of Saudi Arabia; both used creatinine clearance as measurement for renal impairment, which might overestimate the GFR (174), at the time of referral to the nephrologist as an indicator for late referral to nephrology care (99, 175). Therefore, more indications of pre-ESRD nephrology care and its consequences need to be assessed to improve healthcare practice outcomes among patients with CKD.

Aims and scope

The primary aim of this study was to assess pre-ESRD care and to investigate the primary causes of ESRD in two of the most active Ministry of Health (MOH) hospitals in the western region of Saudi Arabia. Pre-ESRD nephrology care was reviewed based on describing multiple indicators including reasons for referral to nephrology care, referral source to nephrology care, pre-ESRD care period, and vascular access type at the first dialysis. The secondary aim was to investigate the potential factors that may be associated with late referral to nephrology care and its consequences. The results of this study may be valuable for providing evidence-based health policy for public health administrators and healthcare providers in Saudi Arabia to prepare a strategy to define and screen people at consistently high risk and to improve rates of early referral to nephrology care, both of which rely upon multidisciplinary demands. These healthcare practices should have a significant impact in the future in decreasing the incidence rate of ESRD, improving the prognosis and quality of life among patients with ESRD before and after initiating RRT, and reducing the burden of healthcare costs.

Methods

Study design and setting

A cross-sectional study was conducted in two large haemodialysis centres in the western region of Saudi Arabia: Alnoor Kidney Centre (AKC), Al Noor Specialist Hospital in the city of Makkah, and Jeddah Kidney Centre (JKC), King Fahad General Hospital in the city of Jeddah. Both are Ministry of Health Hospitals, and are therefore expected to have a similar quality of healthcare services. Data were obtained after applying for ethical approval from the Ministry of Health and General Directorate of Health Affairs in each city.

Study population

Inclusion criteria

Participants were the prevalent patients with ESRD on regular haemodialysis during 2011. This haemodialysis population was chosen for two reasons: according to the Saudi Centre for Organ Transplantation report, they constitute the largest population among patients with RRT in Saudi Arabia (60); and it is easy to locate these patients and extract their medical history and follow-up retrospectively from medical records in dialysis centres, despite the lack of primary care networks and health information systems in Saudi Arabia.

Exclusion criteria

All visiting patients to dialysis centres, who did not have a documented medical history in their medical records, and patients with advanced malignancy were excluded.

Data collection

Electronic medical records were searched to identify all patients with ESRD on haemodialysis in 2011. The total number of patients on haemodialysis in AKC, Al-Noor Specialist Hospital in Makkah was 418, the corresponding number in JKC, King Fahad General Hospital in Jeddah was 634. A simple random sampling technique was used to select a sample of 69 patients from JKC because of time limitations; all patients from AKC were included except for 84 visiting patients to the dialysis centre without a medical history who were excluded. The requested data, including demographic information, date first seen by a nephrologist, reason for referral to a nephrologist, referral source to nephrology care, date of first dialysis, vascular

access used at first dialysis, and causes of ESRD, were collected from medical records and stored in a customised Microsoft Office Access database.

Statistical analysis

Each patient's age at the time of referral to nephrology care and during the pre-ESRD care period were calculated. The pre-ESRD care period was categorised as: 0 months, <6 months, 6-12 months, and >12 months. Reasons for referral to nephrologists were classified using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) and then grouped into the following categories: diseases of the genitourinary system including disorders of the urethra and urinary tract such as haematuria; diseases of the circulatory system including uncontrolled blood pressure; endocrine, nutritional and metabolic diseases and immune disorders including diabetic nephropathy, nephrolithiasis, disorders of fluid electrolyte such as hyperkalaemia and hyperphosphatemia, and unspecified disorders of metabolism; symptoms and signs indicating renal diseases including proteinuria, abnormal creatinine clearance, and eGFR<30; and not reported. Also, primary causes of ESRD were classified according to the ICD-9-CM and grouped into the following categories: diabetes, glomerulonephritis (GN), secondary GN/vasculitis, interstitial nephritis/pyelonephritis, hypertension/large vessel disease, cystic/hereditary/congenital diseases, neoplasms/tumours, and miscellaneous conditions.

Data were analysed descriptively to identify the preliminary indicators of pre-ESRD care and to investigate the primary causes of ESRD. To examine uncertainty, 95% confidence intervals (CIs) were calculated for each outcome. A t-test for two independent samples was performed to examine the association between age at time of referral to nephrology care and sex. A chi-squared or Fisher's exact test was performed to examine the relationship between the pre-ESRD care period and factors that might contribute to late referral to nephrology care practice such as age, sex, referral source, reason for referral to nephrology care, and causes of renal disease; the relationship between the pre-ESRD care period and related healthcare practice outcomes such as the type of vascular access used at first dialysis was also examined. Logistic regression was performed to estimate the effect of potential predictors such as age, sex, referral source, reason for referral to nephrology care, period of pre-ESRD, and causes of renal disease, on the possibility of initiating haemodialysis with AVF as an access point. All analyses were performed using STATA 11.

Results

Patients' characteristics

The total sample size was 403 haemodialysis patients, derived from two dialysis centres: 334 from AKC and 69 from JKC [Figure 3.1]. Males constituted 57.3% of the study population; 93.1% were Saudis. The mean age at time of referral to nephrology care was 44.3 years ($\pm$ standard deviation (SD) 16.4 years). A t-test showed that there was no significant difference between the mean age for males (43.6) and females (45.4) at time of referral to nephrology care with a mean difference of 1.8 years (95%CI: -2.01, 5.8; $p=0.18$). The median period of dialysis care was 4.3 years (25%, 75% percentiles: 2.4, 8.9). A total of 27 patients in the study sample died, and 10 underwent renal transplantation in AKC during 2011. [Table 3.1]

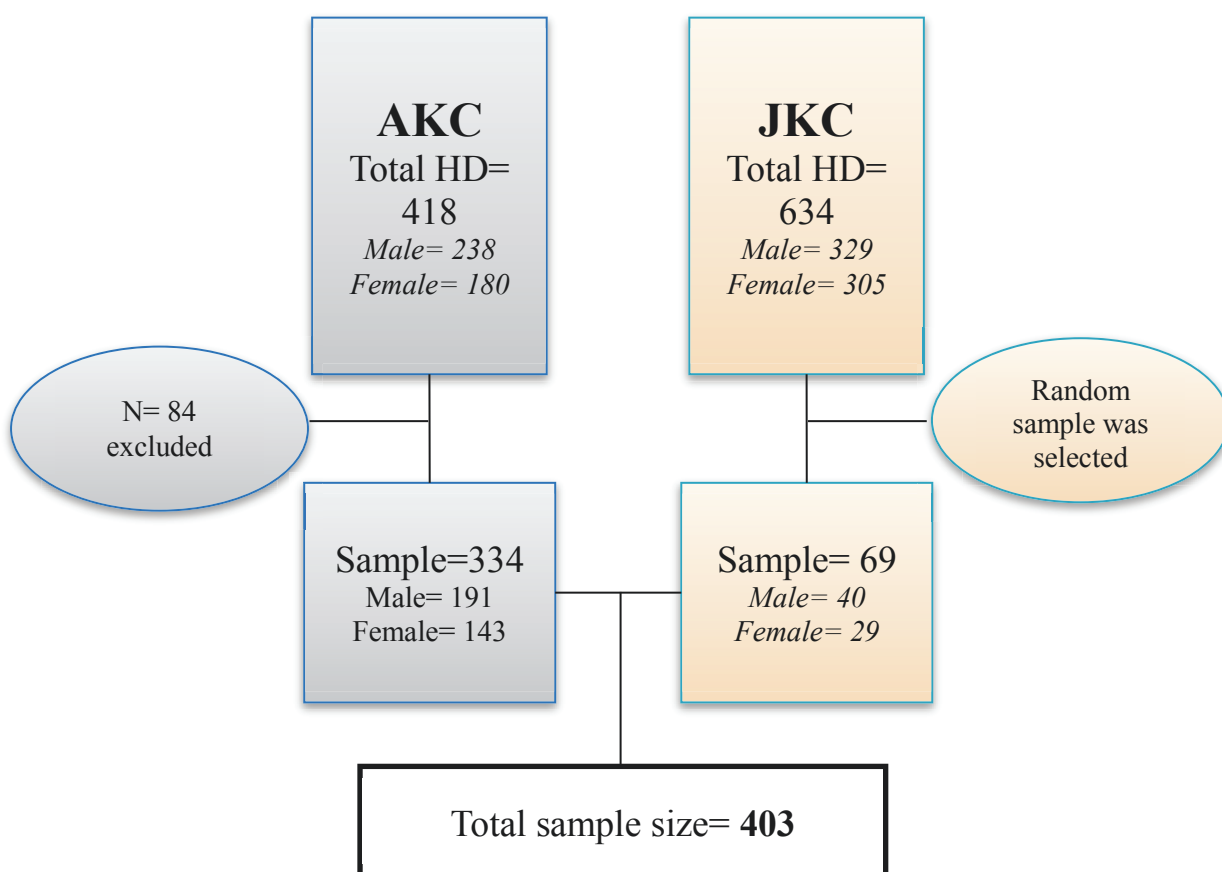


Figure 4.1. Explanation of how the study size was derived.

Preliminary indicators of pre-ESRD care and primary causes of ESRD

In the study sample, the most commonly reported reasons for referral to nephrology care were endocrine, nutritional and metabolic diseases (50.6%), followed by disease of the circulatory system (39.9%), symptoms and signs indicating renal function deterioration (5.9%), and diseases of the genitourinary system (3.6%). In 67 records, the reasons for referral were missing or not reported. Referral from the emergency departments for urgent dialysis served as the principal referral source (50.6%); other sources included outpatient clinics for renal care (27.8%), and different healthcare centres for dialysis (21.6%). The pre-ESRD care period ranged from 0 to 274 months with median 0.06 months (25%, 75% percentiles: 0, 4.7); there were 113 missing records. A total of 47.6% of haemodialysis patients had not received pre-ESRD nephrology care, 28.6% of patients had received care for less than six months, 6.9% received care between six and 12 months, and 16.9% received care for more than 12 months. The principal access point for first dialysis in the study sample was via a catheter (88.3%). Only 8.9% were initiated through an AVF, 2.5% were initiated with an arterio-venous graft and 0.3% were initiated with peritoneal dialysis. To avoid misinterpretation, the trend for AVF and catheter as vascular access at first dialysis was examined [Figure 3.2]. During the last decade, there has been no improvement in referring patients in order to create AVF before first dialysis, and no decrease in the number of patients who have started dialysis with a catheter. This suggests that the rate of early referral practice for patients with CKD at earlier stages to nephrology care has not improved in recent decades. The dominant cause of ESRD was hypertension/large vessel disease (55.8%) followed by diabetes (24.6%), cystic/hereditary/congenital disease (7.2%), GN (6.5%), interstitial nephritis or pyelonephritis (4.5%), and secondary GN/vasculitis (1%), with 0.5% unknown. [Table 3.2].

Factors associated with late referral to nephrology care

There was no statistically significant association between pre-ESRD care period and age ($p=0.06$), sex ($p=0.6$), or causes of renal disease ($p=0.94$). The association between pre-ESRD care period and reason for referral to nephrology care was statistically significant ($p=0.005$), where the majority of patients across all reasons for referral had received no pre-ESRD nephrology care or had received care but for less than six months. There was a significant

association between pre-ESRD care period and referral source ($p<0.0001$), where patients with CKD who had not received pre-ESRD care were often referred from emergency departments for urgent dialysis. Consequently, there was a strong association between pre-ESRD care period and vascular access used at first dialysis ($p<0.0001$), where a large proportion of the study sample had initiated dialysis with a temporal catheter [Table 3.3].

Predictors contributing to initiation of haemodialysis with AVF

The relationship between initiation of haemodialysis with AVF and age and sex was not statistically significant even after adjusting for other predictors including period of pre-ESRD care, reason for referral to nephrology care, cause of renal disease, and referral source. However, there appeared to be a proportional relationship between pre-ESRD care period and initiating haemodialysis with AVF, where a one month unit increase in pre-ESRD care increased the opportunity of CKD patients initiating haemodialysis with AVF by 1%, even after adjusting for other predictors (OR (odds ratio)=1.01; 95%CI: 1.00, 1.02; p -value=0.02). Thus, patients who were referred from different healthcare centres for renal care tended to be around two times more likely to initiate haemodialysis with AVF compared with those who were referred from an emergency department, even after adjusting for other predictors, although this association was not statistically significant (OR=2.30; 95%CI: 0.50, 10.66; $p=0.29$); patients who were referred from outpatients clinics were around six times more likely to initiate haemodialysis with AVF compared with patients who were referred from emergency departments; but after adjusting for other predictors the chance in those patients decreased to around four times (OR=3.99; 95%CI: 1.44, 11.02; p -value=0.008). Also, there was a significant association between the reason for referral to nephrology care and initiating haemodialysis with AVF in the study sample.

Those patients who were referred to nephrology care because of circulatory system diseases were 85% less likely to initiate haemodialysis with AVF compared with patients who were referred to nephrology care because of diseases of the genitourinary system; however, after adjusting for other predictors, they were 81% less likely to initiate haemodialysis with AVF (OR=0.19; 95%CI: 0.04, 0.89; p -value=0.03). The patients who were referred to nephrology care because of endocrine, nutritional and metabolic diseases were 93% less likely to initiate haemodialysis with AVF compared with patients who were referred to nephrology care because of diseases of the genitourinary system; after adjusting for other predictors, they

were 89% less likely to initiate haemodialysis with AVF (OR=0.11; 95%CI: 0.02, 0.51; p-value=0.005). Also, patients who were referred to nephrology care for unknown reasons due to missing data, who had probably been referred from other healthcare centres, were 91% less likely (OR=0.09; 95%CI: 0.01, 0.76; p-value=0.03) to initiate haemodialysis with AVF compared with patients who were referred to nephrology care because of diseases of the genitourinary system. There was no significant association between initiating haemodialysis with AVF and causes of renal disease, despite patients who had ESRD because of diabetic nephropathy being 61% less likely to initiate haemodialysis with AVF (OR=0.39; 95%CI: 0.11, 1.40; p-value=0.15) compared with those patients who had ESRD because of hypertensive nephropathy [Table 3.4].

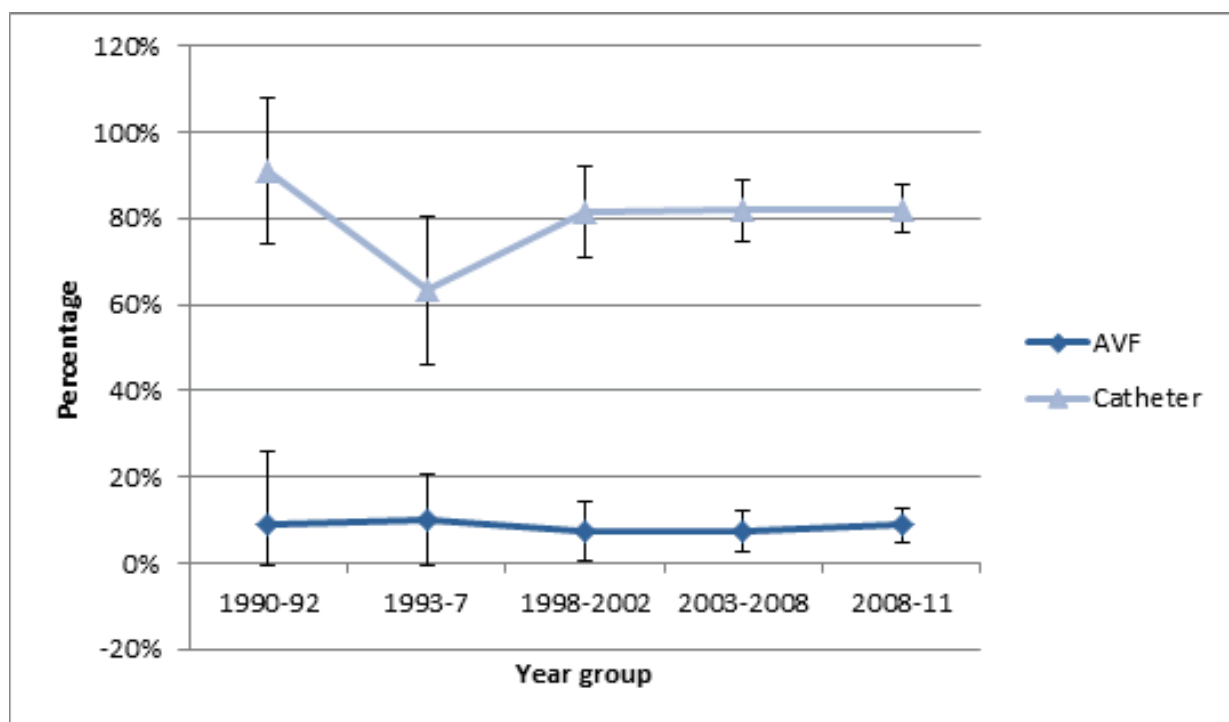


Figure 4.2. Vascular access at first dialysis in recent decades.

AVF= arterio-venous fistula

Table 4.1. Summary of patient characteristics

Patient characteristics	Outcome (N=403)
Patient source	
Alnoor Kidney Centre	334
Jeddah Kidney Centre	69
Age at referral to nephrology care	
Mean (SD)	44.3 ($\pm$ 16.4)
Range	(1.9, 89.7)
Missing	113
Sex (%)	
Male	231 (57.3)
Nationality (%)	
Saudi	375 (93.1)
Period of pre-ESRD care (months)	
Median (25%, 75% percentiles)	0.06 (0, 4.7)
Range	(0, 274.2)
Missing	113
Period of dialysis (years)	
Median (25%, 75% percentiles)	4.3 (2.3, 8.9)
Range	(0.01, 21.2)
Missing	13
Patient status during 2011	
Survived	366
Died	27
Renal transplanted	10

SD= standard deviation.

Table 4.2. Distribution of preliminary indicators of pre-ESRD care and primary causes of ESRD

Outcome	Frequency (N=403)	% (95% CI)
Reason for referral to nephrology care		
Diseases of the genitourinary system	12	3.57 (1.9, 6.2)
Diseases of the circulatory system	134	39.88 (34.6, 45.3)
Endocrine, nutritional and metabolic diseases & immunity disorders	170	50.60 (45.1, 56.1)
Symptoms and signs indicating renal diseases	20	5.95 (3.7, 9.0)
Missing/not reported	67	-
Referral source		
Emergency	204	50.62 (45.6, 55.6)
Outpatient clinic	112	27.79 (23.5, 32.4)
Other healthcare centres	87	21.59 (17.7, 25.9)
Period of pre-ESRD care/month		
0 months (not receiving pre-ESRD care)	138	47.59 (41.7, 53.5)
<6 months	83	28.62 (23.5, 34.2)
6-12 months	20	6.90 (4.3, 10.5)
>12 months	49	16.90 (12.8, 21.7)
Missing/not reported	113	-
Access used at first dialysis		
AVF	32	8.91 (6.2, 12.4)
AVG	9	2.51 (1.2, 4.7)
Catheter	317	88.30 (84.5, 91.3)
PD	1	0.28 (0, 1.5)
Missing/not reported	44	-
Causes of ESRD		
Cystic/hereditary/congenital disease	29	7.2 (4.9, 10.2)
Diabetes	99	24.6 (20.4, 29.1)
Glomerulonephritis	26	6.5 (4.3, 9.3)
Hypertension/large vessel disease	225	55.8 (50.8, 60.7)
Interstitial nephritis/pyelonephritis	18	4.5 (2.7, 7)
Secondary GN/vasculitis	4	1 (0.3, 2.5)
Miscellaneous conditions	2	0.5 (0.1, 1.8)

CI =confidence interval, AVF=arterio-venous fistula, AVG=arterio-venous graft, PD=peritoneal dialysis, GN=glomerulonephritis

Table 4.3. Relationship between pre-ESRD care periods and patient characteristics.

Outcome	Pre-ESRD care period				Total (%)	p-value
	>12m	6-12m	<6m	0m		
Age at time of referral to nephrology care (years)						
<14.9	5	0	1	2	8 (2.76)	
15-29.9	11	3	16	24	54 (18.62)	
30-44.9	14	5	21	43	83 (28.62)	
45-59.9	15	5	28	46	94 (32.41)	
≥60	4	7	17	23	51 (17.59)	0.06
Sex						
Female	20	8	27	57	112 (38.62)	
Male	29	12	56	81	178 (61.38)	0.61
Referral source						
Emergency department	7	6	36	108	157 (54.14)	
Other healthcare centre	11	5	11	17	44 (15.17)	
Outpatient clinic	31	9	36	13	89 (30.69)	<0.0001
Reason for referral to nephrology care						
Diseases of the genitourinary system	4	4	2	1	11 (4.37)	
Diseases of the circulatory system	12	4	31	39	86 (34.13)	
Endocrine, nutritional and metabolic diseases & immunity disorders	19	11	41	69	140 (55.56)	
Symptoms and signs indicating renal diseases	2	0	4	9	15 (5.95)	0.005
Causes of ESRD						
Cystic/hereditary/congenital disease	5	1	6	9	21 (7.24)	
Diabetes	13	7	23	31	74 (25.52)	
Glomerulonephritis	5	1	5	13	24 (8.28)	
Hypertension/large vessel disease	25	11	46	74	156 (53.79)	
Interstitial nephritis/pyelonephritis	1	0	3	7	11 (3.79)	
Secondary GN/vasculitis	0	0	0	2	2 (0.69)	
Miscellaneous conditions	0	0	0	2	2 (0.69)	0.94
Access used at first dialysis						
AVF	14	3	10	0	27 (9.31)	
AVG	2	0	3	3	27 (2.76)	
Catheter	32	17	70	135	254 (87.59)	
PD	1	0	0	0	1 (0.34)	<0.0001

HD=haemodialysis, AVF=arterio-venous fistula, AVG=arterio-venous graft, PD=peritoneal dialysis, GN=glomerulonephritis

Table 4.4. Relationship between initiating haemodialysis with AVF as outcome and different patient characteristics.

Predictor	Unadjusted OR (95% CI)	p-value	Adjusted OR* (95% CI)	p-value
	(N=403)		(N=275)	
Age at time of referral to nephrology care				
Per a year unit	0.99 (0.96, 1.01)	0.29	1.01 (0.97, 1.04)	0.70
Sex				
Female	1	—	1	—
Male	1.17 (0.55, 2.48)	0.68	1.15 (0.46, 2.92)	0.76
Referral source				
Emergency department	1	—	1	—
Other healthcare centre	2.02 (0.62, 6.59)	0.24	2.30 (0.50, 10.66)	0.29
Outpatient clinic	6.31 (2.57, 15.50)	<0.0001	3.99 (1.44, 11.02)	0.008
Period of pre-ESRD care				
Per month unit	1.01 (1.005, 1.02)	0.002	1.01 (1.001, 1.02)	0.02
Reason for referral to nephrology care				
Diseases of the genitourinary system	1	—	1	—
Diseases of the circulatory system	0.15 (0.04, 0.57)	0.005	0.19 (0.04, 0.89)	0.03
Endocrine, nutritional and metabolic diseases & immunity disorders	0.07 (0.02, 0.28)	<0.0001	0.11 (0.02, 0.51)	0.005
Symptoms and signs indicating renal diseases	0.16 (0.02, 1.06)	0.06	0.28 (0.03, 2.24)	0.23
Missing/not reported	0.07 (0.01, 0.36)	0.002	0.09 (0.01, 0.76)	0.03
Causes of ESRD				
Hypertension/large vessel disease	1	—	1	—
Diabetes	0.50 (0.18, 1.38)	0.18	0.39 (0.11, 1.40)	0.15
Glomerulonephritis	1.15 (0.32, 4.17)	0.83	1.15 (0.21, 6.32)	0.87
Cystic/hereditary/congenital disease	0.70 (0.15, 3.18)	0.65	0.47 (0.07, 3.07)	0.43
Interstitial nephritis/pyelonephritis	0.60 (0.07, 4.81)	0.63	—	—
Miscellaneous conditions	—	—	—	—

OR= odds ratio, CI=confidence interval, HD=haemodialysis, AVF=arterio-venous fistula

*Adjusted for age, sex, referral source, period of pre-ESRD care, reason of referral to nephrology care, and causes of ESRD.

Discussion

In Saudi Arabia, the prevalence of risk factors for CKD has risen steadily in recent decades with a corresponding rise in the incidence and prevalence of RRT. In this study, pre-ESRD care and its consequences, and the primary causes of ESRD were reviewed to provide evidence of the quality of healthcare management services before initiating dialysis. The findings related to indicators of pre-ESRD nephrology care in this study show that around 41.7%-53.5% of haemodialysis patients had not received any renal care before initiating dialysis, and around 23.5%-34.2% had received care but for less than six months. This means the risk of morbidity and mortality is increased in these patients, and there is a reduced chance for patients to take part in clinical decisions regarding RRT options. Also, this suggests that there is inadequate time to provide a pre-dialysis educational programme and psychological preparation for patients with CKD, and inadequate time to create a suitable point for permanent vascular access to be used at first dialysis (156, 176-179). This resulted in around 45.6%-55.6% of CKD patients, who progressed to ESRD, being referred from emergency departments for urgent haemodialysis. This in turn led to around 84.5%-91.3% of patients with ESRD having to initiate haemodialysis with a temporary catheter, which is associated with an increased risk of access complications and mortality (164, 166, 169, 180, 181), and only around 6.2%-12.4% of patients having initiated haemodialysis with AVF. However, the NKF-KDOQI and the Renal Association Clinical Practice (RACP) Guidelines on Vascular Access for Haemodialysis recommend that 65% of all incident haemodialysis patients should initiate dialysis with AVF (182, 183). Furthermore, the trend of increasing incidence of haemodialysis patients with AVF has not shown any improvement in recent decades, which implies that the rate of referral of patients with CKD at earlier stages to nephrology care has not been improved, or that patients might have been referred to nephrology care but they were not educated enough about their health condition and its consequences. Although the rate of progression to ESRD for some patients with CKD is unpredictable making timing of access placement difficult, the RACP guidelines recommend that AVF should be placed at a minimum of three months before the expected day of initiating haemodialysis and probably not more than one year (183).

Moreover, this study found that many of the patients (45.1%-56.1%) were referred to nephrology care because of endocrine, nutritional, and metabolic diseases and immunity disorders; and 34.6%-45.3% were referred because of uncontrolled blood pressure. The majority of those

patients had received no nephrology care or the period of care was less than six months, while the dominant causes of ESRD were hypertensive nephropathy (50.8%-60.7%) and diabetic nephropathy (20.4%-29.1%). This implies that the detection and management of the risk factors for CKD including diabetes and hypertension needs to be improved in Saudi Arabia. NKF-KDOQI guidelines states that adverse outcomes of CKD, such as loss of kidney function, kidney failure, and cardiovascular disease, can be prevented or delayed by detecting and treating CKD at earlier stages. This can be done through routine laboratory measurements and eGFR for patients at high risk such as those diagnosed to have hypertension, diabetes, or dyslipidemia, particularly those with an eGFR of less than 60mL/min/1.73m². However, declining eGFR is associated with multiple complications such as hypertension, anaemia, malnutrition, neuropathy, and bone disease. All these complications can be treated at earlier stages of CKD (35, 184, 185).

Limitations

Due to time limitations for collecting data, the lack of a comprehensive national health information system in Saudi Arabia, and some patients being referred from one healthcare centre to another, the laboratory measurements for renal function deterioration and eGFR were not usually available at the time of referral to nephrology care in many medical records and the reason for referral was often insufficiently explained. Furthermore, eGFR could not be calculated to determine at which CKD stage the patient had been referred to nephrology care due to missing or unreported information. The Modification of Diet in Renal Disease (MDRD) study equation to estimate GFR requires taking into account serum creatinine concentration, age, sex, race, and body mass index (35, 174). Therefore, the preliminary indicators for pre-ESRD nephrology care were used in this study for detecting late referral to nephrology care. There is a potential selection bias in terms of the study population due to focusing on haemodialysis patients only. Patients with ESRD who initiated RRT with peritoneal dialysis or had pre-emptive renal transplantation would have been referred to nephrology care at an early stage and received multidisciplinary pre-ESRD education. However, no data were available in the literature on the rate of initiating RRT with peritoneal dialysis or pre-emptive renal transplantation in Saudi Arabia.

Strengths

The indications of pre-ESRD nephrology care in this study provide evidence for public health administrators and healthcare providers in Saudi Arabia to develop multidisciplinary strategies

for improving pre-ESRD nephrology care practice and its outcomes. This study demonstrates that the majority of patients with CKD received no pre-ESRD care or they received less than six months of care across all reasons for referral, and therefore most patients with ESRD were referred from emergency departments for urgent haemodialysis and initiated dialysis with a catheter. Another screening study for CKD, conducted in Riyadh City in Saudi Arabia using eGFR and laboratory measurements to detect CKD in the general population, showed that around 7% of patients with CKD were not aware of their kidney status, 32% had known that they had protein or blood in their urine, and 11% had known that they had kidney stones, but it was not mentioned whether they were followed up by nephrology care services (135). This reflects delayed referral to nephrology care from other services such as primary care, diabetology, and cardiology. Also, where a strong primary healthcare network and health information system is absent, this might reflect that there are many individuals with CKD and its risk factors such as diabetes, hypertension, and cardiovascular disease who are undiagnosed in the general population or who have been diagnosed but not followed up consistently, which may explain why the majority of these individuals are not referred to nephrology care in the early stages of their disease and suddenly progress to ESRD and require urgent dialysis. Therefore, developing strategies to improve the rate of early referral should firstly involve regular screening to detect and manage the risk factors for CKD and CKD in the early stages; this cannot be done efficiently without a comprehensive health information system. Secondly, nephrology departments in healthcare centres should organise campaigns to educate healthcare practitioners including family physicians, diabetologists, cardiologists and internists about the necessity to refer patients with CKD to nephrology care at earlier stages of their illness. Thirdly, improved communication channels are required between healthcare practitioners, as well as defined accurate criteria as to when to refer patients with CKD to nephrology care using a standardised tool (144, 186). Fourthly, healthcare practitioners and social workers should organise programmes to increase patients' awareness about their health status and potential complications. Finally, patients at high risk of ESRD should be trained to better self-manage and be educated about the options of RRT (187). Thus, the rate of referral of patients with CKD at earlier stages to nephrology care and its outcomes should be improved.

Comparisons

By comparing the findings of this study with similar publications that were conducted in Saudi Arabia which used the level of serum creatinine clearance at time of referral to nephrology care to indicate late referral (99, 175), all studies suggested that healthcare practitioners should be aware about when they have to refer patients with CKD to nephrology care, in order to provide optimal pre-ESRD care.

Conclusion

This study provides evidence about the current status of pre-ESRD care in Saudi Arabia and suggests that the rate of early referral of patients with CKD to nephrology care must be improved in order to prevent or delay the progression of renal disease to ESRD. Communications between healthcare practitioners, and collaborations between primary and secondary healthcare professionals should be encouraged, to provide optimal pre-ESRD care including health education for patients about their illness and its consequences, giving patients the chance to consider and decide between RRT options, and allow time to create a permanent vascular access point for dialysis. Further prospective studies are needed to evaluate pre-ESRD care practice and its outcomes in order to implement the best intervention that will help to improve pre-ESRD care practice outcomes in Saudi Arabia.

CHAPTER 5

Review of the indications for hospitalisation among haemodialysis patients in Saudi Arabia

Abstract

Background

The high cost of hospitalisation for haemodialysis patients has become a public health concern because increases in the haemodialysis population together with escalating healthcare costs are not sustainable worldwide. In Saudi Arabia, the haemodialysis population has increased continuously in the last three decades with a high prevalence of co-morbid conditions and complications that are related to haemodialysis procedures. The indications for hospitalisation usually reflect either the quality of healthcare services, or the severity of patients' co-morbid conditions.

Aims

This study was conducted to review the indications for hospitalisations which are associated with an increased cost of healthcare and reflect the severity of co-morbid conditions by investigating; (I) the primary causes for hospital admissions, (II) the primary causes for hospital admissions which are associated with an increase in length of stay in hospital, (III) the potential factors that might increase the number of hospital admissions among haemodialysis patients.

Methods

A retrospective cohort study was conducted in the Alnoor Kidney Centre in Al Noor Specialist Hospital, Makkah City, Saudi Arabia, which is a Ministry of Health hospital. Participants were prevalent patients with end-stage renal disease on regular haemodialysis in 2011, who had

received haemodialysis for more than three months. Each patient had been followed-up retrospectively, from the first date of initiating haemodialysis to the end of 2011.

Results

The most common reasons for hospitalisation among haemodialysis patients were diseases of the genitourinary system (40.1%; 95% CI: 35.7%, 44.6%), diseases of the circulatory system (22.6%; 95% CI: 19%, 26.6%), vascular access (19.5%; 95% CI: 16.1%, 23.4%), infectious diseases (9%; 95% CI: 6.6%, 12%), and endocrine and metabolic diseases (7.4%; 95% CI: 5.2%, 10.1%). The primary reason for hospital admissions associated with increases in the length of stay in hospital, were diseases of the circulatory system (which increased hospital bed days by 70%; 95% CI: 11% to 161%; p-value=0.01 compared to all other reasons). The risk factors that increased the rate of hospital admissions per patient-year at risk were increasing age (IRR=1.02; 95% CI: 1.01, 1.03; p-value=<0.0001); receiving haemodialysis through a catheter compared to arterio-venous fistula (IRR=2.55; 95% CI: 1.14, 4.97; p-value=0.0009); and diabetes as a cause of renal disease compared to hypertension (IRR=1.84; 95% CI: 1.29, 2.63; p-value=0.001).

Conclusion

Indications for hospitalisation and consequences of practices related to hospitalisation for haemodialysis patients should be studied in further researches to provide a comprehensive evidence-based health policy for haemodialysis patients in Saudi Arabia.

Background

The high cost of hospitalisation for haemodialysis patients has become a public health concern (188, 189) because an increase in the haemodialysis population together with escalating healthcare costs are not sustainable worldwide (139, 190, 191). The United States Renal Data System (USRDS) report highlighted that the rates of hospital readmissions for end-stage renal disease (ESRD) patients are twice those in the general Medicare population (192). Patients with chronic kidney disease (CKD) in late stages are often hospitalised with general medical problems, especially those patients who have reached the end-stage of renal failure and are receiving regular haemodialysis in dialysis centres (193-195). Patients on haemodialysis require more resources than patients on peritoneal dialysis or with renal graft

need, especially during the first year of dialysis treatment; these resources include vascular surgery, radiology, physician cost, and hospitalisation (169, 188, 196-199).

In Saudi Arabia, the incidence and prevalence of the renal replacement therapy (RRT) population have been increasing continuously in the last three decades with a high prevalence of co-morbid conditions (60, 200) and complications related to ESRD (27, 173). The most common method for treating patients with ESRD in recent decades has been haemodialysis, which accounts for just over half of the RRT population. The Ministry of Health (MOH) in Saudi Arabia incurs the vast majority of haemodialysis care costs, and provides around two-thirds of haemodialysis facilities. Although the ESRD population accounted for only 0.08% of the total Medicare population in Saudi Arabia in 2008, it is estimated that the healthcare costs associated with those patients were around 3.8% of the total MOH expenditure (27). In the United States, the ESRD population accounts for 0.5% of the total Medicare population, but the cost of ESRD care contributes to 5% of Medicare expenses (201); hospitalisation accounts for around 41% of the total ESRD care costs (202); and in the period between 1999 and 2004, the cost of ESRD care had risen to 6.7% with a corresponding increase in the ESRD population of 0.03% in 2004 (139).

In order to provide comprehensive renal care services for patients on haemodialysis, a study demonstrated that the risk of readmission, length of stay in hospital, and the average cost of haemodialysis care tended to be lower for patients under the care of nephrologists compared to internists (189). The British Renal Society (BRS) National Renal Workforce Planning Group (2002) recommended that one whole-time equivalent renal physician is required for 75 to 100 patients on RRT (203), while in Saudi Arabia one consultant nephrologist will be required for 234 patients on RRT by 2015 (27). Furthermore, patients with ESRD who had received pre-ESRD care by nephrologists before initiating haemodialysis had a better outcome throughout haemodialysis with a reduced risk of hospitalisation and mortality compared to those patients who had not received nephrology care (170, 204-206). However, in Saudi Arabia, a large proportion of haemodialysis patients do not receive pre-ESRD care (99).

The risk of hospitalisation increases among patients on haemodialysis due to complications of either haemodialysis (207, 208) or haemodialysis vascular access (209, 210), with a high prevalence of co-morbid conditions particularly diabetes (211) and cardiovascular diseases (212-214). The type of vascular access used in the dialysis process makes a significant

contribution to prognosis and quality of life (215-220). Many studies have shown that using a catheter at the initiation of haemodialysis or throughout the time on haemodialysis increases the risk of hospitalisation, particularly due to catheter related infection (221, 222). Conversions from catheter to arteriovenous fistula (AVF) have lowered the risk of hospitalisation among haemodialysis patients (164, 223-226). In Saudi Arabia, there is limited literature on studies of the risk of hospitalisation among haemodialysis patients particularly that associated with vascular access practice patterns. A few studies conducted in different areas of Saudi Arabia have shown that a large proportion of incident ESRD patients initiated haemodialysis treatment with a temporary catheter as a result of a late referral to nephrology care, a practice which is associated with increased morbidity and mortality (227, 228), and increased costs of healthcare.

Diabetes is a costly condition and a substantial amount of money is spent annually worldwide to treat diabetes complications such as diabetic nephropathy and coronary artery disease, while a large proportion of the total cost is spending for hospitalisation (115, 229). Diabetic nephropathy is a common and often severe complication among diabetic patients; it is also related to an increased economic burden of ESRD care (211, 230, 231). Several studies have shown that age and diabetes are major risk factors for coronary artery disease (232-234), which is a major cause of cardiac hospitalisation and death among haemodialysis patients (205, 235). The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF/KDOQI) and the American Heart Association have stated that patients with CKD are considered to be in the highest risk group for cardiovascular disease events compared to the general population (35, 236), particularly coronary artery disease which is a major cause of cardiac hospitalisation and death among haemodialysis patients (205, 235). Saudi Arabia is one of the leading countries for diabetes prevalence in the world (237, 238) and therefore, diabetic nephropathy contributes significantly to renal disease, as the reported incidence of ESRD due to diabetic nephropathy in Saudi Arabia is also one of the highest in the world (27, 60, 115, 200).

The indications for hospitalisation among haemodialysis patients usually reflect either the quality of healthcare services, or the severity of patients' co-morbid conditions, which may be associated with increasing hospital utilisation and healthcare costs. Only two studies in the literature have reported the period prevalence of the primary reasons for hospitalisation

among the haemodialysis population in Saudi Arabia. The first study conducted in Riyadh City reported cardiovascular disease as the primary reason for hospitalisation, followed by vascular access complications and infections (115). The second study conducted in Al-Madinah City reported vascular access related problems as the primary reason, followed by infectious disease and cardiovascular disease (38). Neither study reported the risk factors that might increase the rate of hospital admissions or the length of stay in hospital per patient-year on haemodialysis, which are usually reflections of the severity of patients' co-morbid conditions and the quality of healthcare services.

Aims and scope

This study was conducted in one of the most active MOH hospitals in Makkah City in Saudi Arabia. The aims were to review the primary reasons and other indications for hospital admissions among patients with ESRD on haemodialysis. This would provide evidence-based health policy that may help to improve the quality of healthcare services where possible and meet the increasing demand for healthcare services among haemodialysis patients in Saudi Arabia. I also aimed to identify the priority areas for further healthcare services research that may help to reduce the rate of admission and length of stay in hospital in the future. The review of indications for hospital admission among haemodialysis patients, were performed by investigating the following:

- The primary reasons for hospital admissions among patients with ESRD after starting haemodialysis
- The reasons for hospital admissions associated with an increase in the length of stay in hospital.
- The risk factors associated with an increase in the rate of number of hospital admissions after starting haemodialysis

Methods

Study design and setting

A retrospective cohort study was conducted in the Alnoor Kidney Centre (AKC) in Al Noor Specialist Hospital, which is the largest Ministry of Health Centre in Makkah City in the

western region of Saudi Arabia. Data were obtained after applying for ethical approval from the Ministry of Health and General Directorate of Health Affairs in Makkah.

Study population

Inclusion criteria

Participants were prevalent patients with ESRD on regular haemodialysis in 2011, who had received haemodialysis for more than three months. Each patient had been followed up retrospectively since the day after the first date of initiating haemodialysis until the end of 2011.

Exclusion criteria

All visiting patients to the dialysis centre who did not have a documented medical history in medical records and patients with advanced malignancy were excluded.

Data collection

Electronic medical records were searched to identify all patients with ESRD on haemodialysis in 2011. The total number of patients on haemodialysis was 418. A further 84 patients visiting the dialysis centre without a medical history and 16 patients who had received haemodialysis for less than three months were excluded.

The requested data including demographic information (age at onset of dialysis, sex, nationality), date of starting dialysis, patient status throughout 2011 (survived, renal transplant, died), causes of renal disease (diabetic nephropathy, hypertensive nephropathy, glomerulonephritis, other), vascular access (access type at first dialysis, access type during follow-up), co-morbid conditions (diabetes, hypertension, ischaemic heart disease, congestive heart failure, cerebrovascular disease, peripheral vascular disease, pulmonary disease, neurologic disease, gastrointestinal bleeding, hepatitis B virus (HBV), hepatitis C virus (HCV), catheter related infection), limitation in physical motion, ever received blood transfusion, and hospitalisation (causes of admission, dates of admission and discharge) were collected from medical records and stored in a customised Microsoft Office Access database.

Statistical analyses

The total number of hospital admissions (excluding admissions on the day that haemodialysis was started) and the time on haemodialysis in years were calculated for each patient, and the length of stay in hospital was calculated for each hospitalisation. Admissions for less than one night observation were excluded from the analysis. The primary causes for hospital admissions were classified using ICD-10 codes updated in 2011, and were grouped into the following diagnostic categories for analyses: non-infectious diseases including anaemia, diseases of the musculoskeletal system, diseases of the digestive system, endocrine and metabolic diseases, diseases of the nervous system, diseases of the respiratory system, diseases of the genitourinary system, diseases of the circulatory system, diseases of the skin, vascular access, trauma or injury related conditions, and miscellaneous; and overall infectious diseases including sepsis, infections of the skin and subcutaneous tissue, infectious arthropathies, respiratory infectious disease, other infectious disease, and viral infection. [Appendix C]

Data were analysed descriptively to describe patients' characteristics, co-morbid conditions, and the distribution of the most frequent causes of hospital admissions after starting haemodialysis in the study sample. Negative Binomial regression was used among patients who were hospitalised at least once, clustered hospital admissions data by patients' identity numbers to investigate which primary reasons for hospital admissions were associated with the greatest number of hospital bed days per patient-year on haemodialysis. This is adjusted for patients' characteristics at onset of haemodialysis such as age, sex, and causes of renal disease. Negative Binomial regression was also used amongst all patients to investigate the risk factors associated with an increase in the number of hospital admissions during time on haemodialysis, clustered by patient. This estimates the IRR of the number of hospital admissions per patient-year at risk for vascular access type during follow-up, and for causes of renal disease, adjusted for age, and sex. An equivalent model was created to examine the effect of vascular access type at start of dialysis, with the same covariates. All analyses were performed using STATA 11 (StataCorp, College Station, TX, USA).

Results

Patients characteristics

The total number of patients on regular haemodialysis was 318: 208 patients were hospitalised at least once, and 110 patients did not have any reported hospitalisation in Al Noor Specialist Hospital [Figure 4.1]. The median period of haemodialysis care (period of follow-up) was 4.3 years (25%, 75% percentiles: 2.4, 8.7), and around 8.2% of patients (26/318) had received haemodialysis for one year or under. The study sample was composed of 58.2% males and 93.7% Saudis. The mean age at onset of dialysis was 45.6 ($\pm$ standard deviation (SD)=16.9) years. The dominant cause of renal disease in the study sample was hypertensive nephropathy (58.8%), followed by diabetic nephropathy (23.9%), and glomerulonephritis (4.1%). Haemodialysis was initiated through a catheter in 80.2% of patients; only 7.2% initiated haemodialysis through an AVF. In 2011, the type of vascular access appeared to have been replaced for the majority of patients after starting haemodialysis. The proportion of prevalent patients with a catheter decreased to around 3.8%, and of those with an AVF, increased to around 95%. The prevalence of co-morbid conditions was high, particularly for diabetes (24.8%) and cardiovascular diseases including hypertension (75.2%), ischaemic heart disease (8.5%), congestive heart failure (6.3%), cerebrovascular disease (3.1%), and peripheral vascular disease (2.5%). The prevalence of HBV was 8.5%, while the prevalence of HCV was very high, around 47.5%. The prevalence of the occurrence of catheter related infection in the study population was 3.1%. A limitation in physical movement was found in 41.5% of patients, and 23% had received a blood transfusion. [Table 4.1] In 2011, 25 (7.9%) patients in the study sample died and 10 patients underwent renal transplantation although eight of them were rejected. The dominant causes of death were cardiovascular disease (7 patients) and sepsis (7 patients), followed by cerebrovascular accident (2 patients), cardiac arrest (2 patients), and death due to unknown or unreported reasons (7 patients).

Primary reasons for hospital admissions and length of stay in hospital

There were 486 recorded hospital admissions for 208 haemodialysis patients in the study sample. The length of stay in hospital ranged between one and 80 days per hospital admission with a median of three days per admission (25%, 75% percentiles: 2, 6).

Distribution of the primary reasons for hospital admissions

The most frequent reasons for hospitalisation throughout the follow-up period in the study sample were diseases of the genitourinary system (40.1%), diseases of the circulatory system (22.6%), and vascular access (19.5%), followed by overall infectious diseases (9%), endocrine and metabolic diseases (7.4%), diseases of the digestive system (5.6%), diseases of the respiratory system (3.1%), diseases of the nervous system (1.8%), diseases of the musculoskeletal system (1.4%) and diseases of the skin (0.2%).

Regarding diseases of the circulatory system, the most frequent cause of admissions was hypertensive disease (9.3%), followed by ischaemic heart disease (6.4%), other forms of heart disease (3.9%), cerebrovascular disease (1.8%), and peripheral vascular disease (1.2%). The majority of patients in the study sample initiated dialysis with a catheter as vascular access for haemodialysis which was often replaced by AVF during the first year of follow-up; therefore, the percentage of hospitalisations as a result of creating a permanent vascular access (14.8%) was higher than the percentage of hospitalisations due to complications (other than related infection) of vascular access (4.5%). For hospital admission due to overall infectious diseases, the most frequent admission was because of respiratory infectious diseases (3.5%), followed by infections of the skin and subcutaneous tissue (2.7%), and sepsis (1.4%). The highest percentage of hospital admissions due to endocrine and metabolic diseases was for metabolic disorders (5.1%), followed by disorders of the endocrine gland (1.6%) and diabetes mellitus (0.62%). [Table 4.2]

Reasons for hospital admissions associated with an increase in the length of stay in hospital per patient-year on haemodialysis

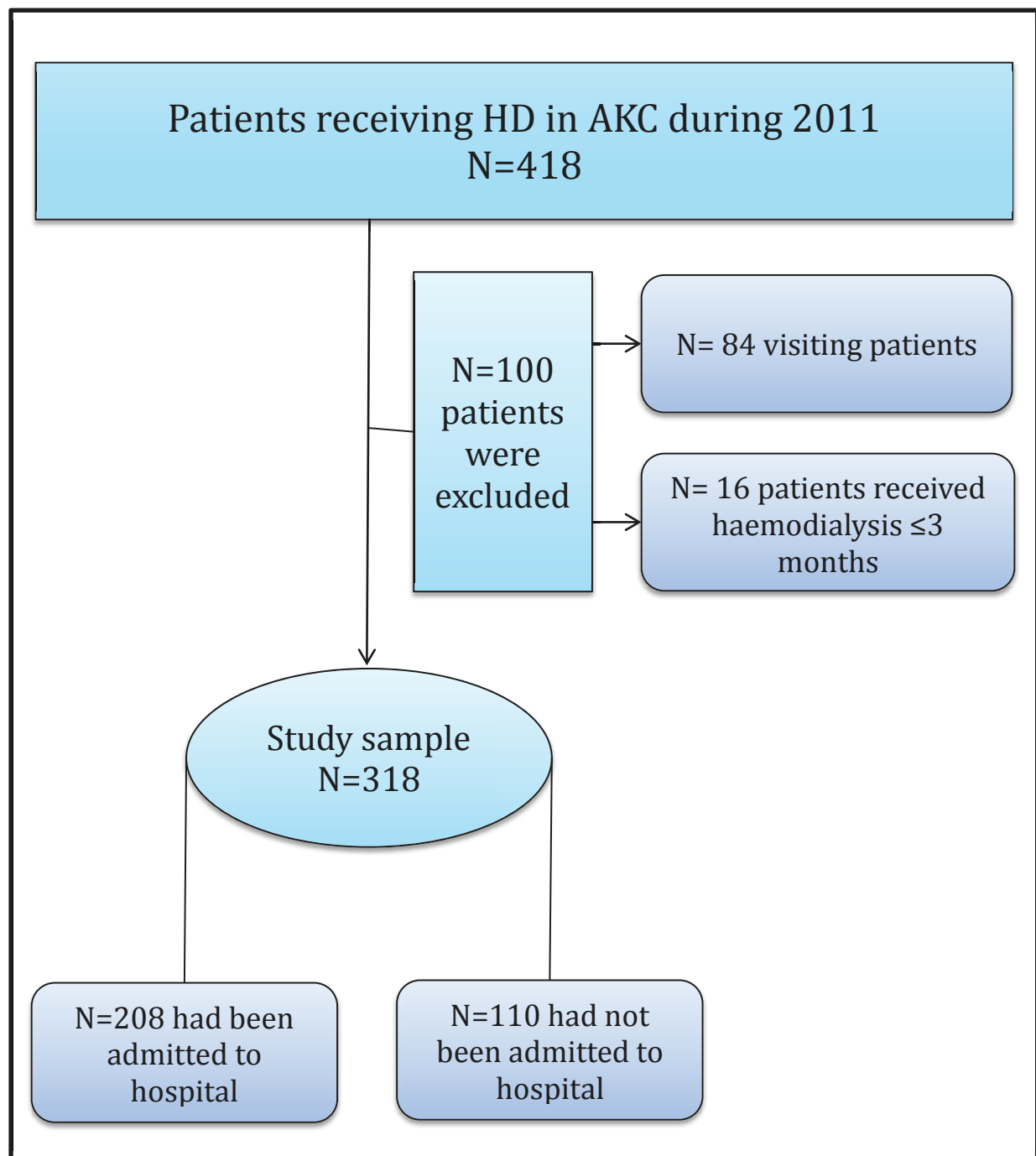
The adjusted ratios of mean number of bed days in hospital per patient-year on haemodialysis show that hospital admissions for diseases of the circulatory system increased the number of hospital bed days per patient-year on haemodialysis by 70% compared to other reasons for hospital admissions. Hospitalisations for diseases of the genitourinary system, for diseases of the nervous system, for trauma/ injury and for vascular access creation all resulted in lower mean hospital days per person-year on dialysis, compared to other reasons for hospitalisation. Note that vascular access procedures are usually required for haemodialysis patients during the first year of dialysis if the patient had haemodialysis initiated with a catheter [Table 4.3]. There was a proportional relationship between the

number of hospital bed days per patient-year on haemodialysis and patient age for all reasons for admission, and the adjusted rate of length of stay in hospital per patient-year at risk increased by around 2% per a year increase in patient age. Sex and causes of renal disease did not have any significant effect on the length of stay in hospital for any disease [Table 4.4].

Factors that increase the risk of hospital admissions per patient-year on haemodialysis

The number of admissions for 318 patients in the study sample ranged between 0 and 17 admissions per patient during the follow-up period, with median=1 hospital admission per patient (25%, 75% percentiles: 0, 2). The potential risk factors at baseline analysis, which might be associated with an increase in the number of admissions per patient-year on haemodialysis, were investigated. The findings from Model_2 show that the rate of the expected number of hospital admissions increased by 2% per patient-year at risk with a one year increase in age, while there was no significant effect for sex on the rate of number of admissions. Patients who received haemodialysis through a catheter during the follow-up period showed an increase in the rate of the expected number of hospital admissions by 2.55 fold per patient-year at risk compared to those patients who received haemodialysis through an AVF. Patients who had ESRD because of glomerulonephritis or diabetic nephropathy also showed an increase in the rate of the expected number of admissions by 2.28-fold and 1.84-fold respectively, compared to those patients who had ESRD because of hypertensive nephropathy, while the unadjusted IRR for the relationship between the number of admissions and glomerulonephritis as a cause of ESRD was not statistically significant. In Model_1, the estimated IRRs for hospital admissions show that the effect of age, sex, and causes of renal diseases are similar to those in Model_2. However, using a catheter at initiation of haemodialysis tends to increase the risk of hospital admission by 62% per patient-year at risk, although this relation was not statistically significant. [Table 4.5]

Figure 5.1. Recruitment of study participants



HD=haemodialysis

Table 5.1. Characteristics of study participants

Patient characteristics	Outcome (N=318 patients)
Demographics	
Mean age in years (SD)	45.6 (±16.9)
Male (%)	185 (58.18)
Saudi (%)	298 (93.7)
Access type at start of dialysis (%)	
AVF	23 (7.23)
AVG	7 (2.2)
Catheter	255 (80.19)
PD	1 (0.31)
Missing	32 (10.06)
Access type during follow-up (%)	
AVF	302 (94.97)
AVG	4 (1.26)
Catheter	12 (3.77)
Period of haemodialysis (years)	
Median (25%, 75% percentiles)	4.3 (2.4, 8.7)
Cause of renal disease (%)	
Diabetes	76 (23.9)
Glomerulonephritis	13 (4.09)
Hypertension	187 (58.81)
Other	42 (13.21)
Comorbid conditions (%)	
Diabetes	79 (24.8)
Hypertension	239 (75.2)
Ischaemic heart disease	27 (8.5)
Congestive heart failure	20 (6.3)
Cerebrovascular disease	10 (3.1)
Peripheral vascular disease	8 (2.5)
Pulmonary disease	22 (6.9)
Neurologic disease	11 (3.5)
Gastrointestinal bleeding	3 (0.9)
Hepatitis B virus	27 (8.5)
Hepatitis C virus	151 (47.5)
Catheter related infection	10 (3.14)
Limitation in physical motion (%)	132 (41.51)
Ever received blood transfusion (%)	73 (23)

AVF=arteriovenous fistula, AVG=arteriovenous graft, PD=peritoneal dialysis

Table 5.2. Distribution of hospital admissions by diagnostic categories

Cause of hospitalisation	Frequency (N= 486 admissions)	% (95% CI)
Anaemia	8	1.65 (0.71, 3.22)
Diseases of the circulatory system	110	22.63 (18.99, 26.62)
<i>Hypertensive disease</i>	45	9.26 (6.83, 12.19)
<i>Ischaemic heart disease</i>	31	6.38 (4.37, 8.93)
<i>Other forms of heart disease</i>	19	3.91 (2.37, 8.93)
<i>Cerebrovascular disease</i>	9	1.85 (0.85, 3.49)
<i>Vascular disease</i>	6	1.23 (0.45, 2.67)
Diseases of the digestive system	27	5.56 (3.69, 7.98)
Diseases of the genitourinary system	195	40.12 (35.73, 44.63)
Diseases of the musculoskeletal system	7	1.44 (0.58, 2.94)
Diseases of the nervous system	9	1.85 (0.85, 3.49)
Diseases of the respiratory system	15	3.09 (1.7, 5.03)
Diseases of the skin	1	0.21 (0.005, 1.14)
Endocrine and metabolic diseases	36	7.41 (5.24, 10.11)
<i>Diabetes mellitus</i>	3	0.62 (0.13, 1.79)
<i>Disorders of endocrine glands</i>	8	1.65 (0.71, 3.22)
<i>Metabolic disorders</i>	25	5.14 (3.36, 7.50)
Miscellaneous	7	1.44 (0.58, 2.94)
Overall infectious diseases	44	9.05 (6.65, 11.96)
<i>Sepsis</i>	7	1.44 (0.006, 2.94)
<i>Infections of the skin and subcutaneous tissue</i>	13	2.67 (1.43, 4.53)
<i>Infectious arthropathies</i>	4	0.82 (0.22, 2.10)
<i>Intestinal infectious diseases</i>	1	0.21 (0.00005, 1.14)
<i>Respiratory infectious diseases</i>	17	3.5 (2.05, 5.54)
<i>Viral infection</i>	3	0.62 (0.13, 1.79)
<i>Other infectious diseases</i>	3	0.62 (0.13, 1.79)
Trauma or injury related condition	3	0.62 (0.13, 1.79)
Vascular access	95	19.55 (16.11, 23.36)
<i>Complications</i>	22	4.53 (2.86, 6.77)
<i>Creation</i>	72	14.81 (11.77, 18.29)

Table 5.3. The ratio of the mean number of hospital bed days per patient-year on dialysis for each cause of hospital admission in turn, compared all other disease groups combined.

	Unadjusted ratios of mean number of bed days per patient-year at risk (95% CIs)	p-value	Adjusted ratios of mean number of bed days per patient-year at risk (95% CIs)*	p-value
Cause of hospitalisation	(N=208 patients)		(N=208 patients)	
Anaemia	0.74 (0.39, 1.43)	0.38	0.92 (0.57, 1.49)	0.75
Diseases of the circulatory system	1.62 (0.97, 2.71)	0.07	1.70 (1.11, 2.61)	0.01
<i>Diseases not of the circulatory system</i>	1	—	1	—
<i>Hypertensive disease</i>	1.53 (0.73, 3.24)	0.26	1.76 (0.97, 3.21)	0.06
<i>Ischaemic heart disease</i>	2.05 (0.70, 6.07)	0.19	2.07 (0.90, 4.77)	0.09
<i>Other forms of heart disease</i>	1.66 (0.78, 3.52)	0.19	1.56 (0.81, 3.02)	0.18
<i>Cerebrovascular disease</i>	0.79 (0.30, 2.10)	0.64	0.66 (0.30, 1.46)	0.31
<i>Vascular disease</i>	1.27 (0.69, 2.32)	0.44	1.50 (0.83, 2.70)	0.17
Diseases of the digestive system	0.98 (0.58, 1.66)	0.94	0.95 (0.59, 1.55)	0.85
Diseases of the genitourinary system	0.69 (0.51, 0.95)	0.02	0.71 (0.54, 0.94)	0.02
Diseases of the musculoskeletal system	1.78 (0.53, 5.98)	0.35	2.51 (0.58, 10.93)	0.22
Diseases of the nervous system	0.65 (0.35, 1.22)	0.18	0.49 (0.27, 0.86)	0.01
Diseases of the respiratory system	0.70 (0.30, 1.61)	0.4	0.63 (0.29, 1.40)	0.26
Endocrine and metabolic diseases	0.94 (0.44, 2.01)	0.88	0.87 (0.51, 1.47)	0.6
<i>Non-endocrine, non-metabolic disease</i>	1	—	1	—
<i>Diabetes mellitus</i>	0.53 (0.27, 1.04)	0.06	0.50 (0.26, 0.98)	0.04
<i>Disorders of endocrine glands</i>	0.41 (0.24, 0.70)	0.001	0.36 (0.21, 0.63)	<0.0001
<i>Metabolic disorders</i>	1.20 (0.51, 2.85)	0.68	0.11 (0.62, 2.01)	0.72
Miscellaneous	0.44 (0.14, 1.38)	0.16	0.39 (0.14, 1.06)	0.07
Overall infectious diseases	1.13 (0.68, 1.87)	0.65	1.06 (0.72, 1.57)	0.76
<i>Non-infectious diseases</i>	1	—	1	—
<i>Sepsis</i>	0.96 (0.35, 2.62)	0.94	0.95 (0.43, 2.07)	0.9
<i>Infections of the skin and subcutaneous tissue</i>	1.54 (0.57, 4.18)	0.4	1.12 (0.61, 2.07)	0.7
<i>Infectious arthropathies</i>	0.91 (0.50, 1.65)	0.75	1.16 (0.50, 2.71)	0.73
<i>Respiratory infectious diseases</i>	1.10 (0.36, 3.36)	0.87	0.96 (0.47, 1.98)	0.92
<i>Viral infection</i>	1.05 (0.33, 3.35)	0.94	1.36 (0.58, 3.21)	0.48
<i>Other infectious diseases</i>	0.93 (0.49, 1.77)	0.83	0.87 (0.46, 1.68)	0.69
Trauma or injury related condition	0.31 (0.22, 0.44)	<0.0001	0.26 (0.14, 0.49)	<0.0001
Vascular access	0.70 (0.48, 1.01)	0.06	0.70 (0.51, 0.97)	0.03
<i>Non-vascular access causes</i>	1	—	1	—
<i>Complications</i>	1.08 (0.51, 2.31)	0.84	0.91 (0.52, 1.58)	0.74
<i>Creation</i>	0.61 (0.43, 0.87)	0.007	0.64 (0.45, 0.91)	0.01

CIs=Confidence intervals, *Adjusted for age, sex, and causes of renal disease.

Table 5.4. A - Adjusted ratio of the mean number of hospital bed days per patient-year on dialysis by patient characteristics at baseline. Data is analysed separately for each reason for hospital admissions in turn

Predictors	Anaemia	Diseases of the circulatory system	Diseases of the digestive system	Diseases of the genitourinary system	Diseases of the musculo-skeletal system	Diseases of the nervous system
Ratios of mean number of hospital bed days per patient year on dialysis (95% CIs)						
Age						
<i>Per year</i>	1.02 (1.01, 1.04)	1.02 (1.01, 1.03)	1.02 (1.01, 1.04)	1.02 (1.01, 1.03)	1.02 (1.01, 1.03)	1.02 (1.01, 1.04)
Sex						
<i>Female</i>	1	1	1	1	1	1
<i>Male</i>	0.91 (0.65, 1.28)	0.92 (0.67, 1.27)	0.91 (0.65, 1.28)	0.95 (0.68, 1.34)	0.95 (0.68, 1.34)	0.90 (0.64, 1.27)
Cause of renal disease						
<i>Hypertension</i>	1	1	1	1	1	1
<i>Glomerulonephritis</i>	1.5 (0.50, 3.84)	1.51 (0.54, 4.26)	1.51 (0.59, 3.84)	1.51 (0.60, 3.83)	1.51 (0.60, 3.83)	1.52 (0.60, 3.81)
<i>Diabetes</i>	1.36 (0.87, 2.13)	1.40 (0.94, 2.10)	1.36 (0.87, 2.13)	1.40 (0.92, 2.14)	1.40 (0.92, 2.14)	1.37 (0.87, 2.15)
<i>Others</i>	1.44 (0.92, 2.27)	1.33 (0.87, 2.04)	1.44 (0.92-2.27)	1.38 (0.89, 2.14)	1.38 (0.89, 2.14)	1.44 (0.92, 2.26)

Table 4.4. *B - Adjusted ratio of the mean number of hospital bed days per patient-year on dialysis by patient characteristics at baseline. Data is analysed separately for each reason for hospital admissions in turn*

Predictors	Diseases of the respiratory system	Endocrine and metabolic diseases	Vascular access	Overall infectious diseases	Miscellaneous	Trauma or injury related condition
Ratios of mean number of hospital bed days per patient year on dialysis (95% CIs)						
Age						
<i>Per year</i>	1.02 (1.01, 1.04)	1.02 (1.01, 1.04)	1.02 (1.01, 1.04)	1.02 (1.01, 1.04)	1.02 (1.01, 1.04)	1.02 (1.01, 1.04)
Sex						
<i>Female</i>	1	1	1	1	1	1
<i>Male</i>	0.91 (0.64, 1.27)	0.90 (0.64, 1.27)	0.93 (0.66, 1.30)	0.91 (0.65, 1.28)	0.91 (0.65, 1.28)	0.91 (0.65, 1.28)
Cause of renal disease						
<i>Hypertension</i>	1	1	1	1	1	1
<i>Glomerulonephritis</i>	1.57 (0.60, 4.09)	1.50 (0.59, 3.81)	1.52 (0.63, 3.66)	1.51 (0.60, 3.76)	1.52 (0.60, 3.83)	1.51 (0.59, 3.84)
<i>Diabetes</i>	1.38 (0.88, 2.17)	1.35 (0.86, 2.11)	1.38 (0.89, 2.13)	1.36 (0.86, 2.16)	1.38 (0.88, 2.17)	1.37 (0.88, 2.15)
<i>Others</i>	1.45 (0.93, 2.28)	1.45 (0.92, 2.28)	1.42 (0.91, 2.22)	1.44 (0.92, 2.27)	1.46 (0.93, 2.29)	1.46 (0.93, 2.30)

Table 5.5. Incidence rate ratio of the number of admissions per patient-year on dialysis

Predictors	Unadjusted IRR (95% CI) (N= 318 patients)	p-value	*Adjusted IRR (95% CI) (N= 286 patients)	p-value	**Adjusted IRR (95% CI) (N= 318 patients)	p-value
Age						
<i>Per year of age</i>	1.02 (1.01, 1.03)	0.001	1.02 (1.01, 1.03)	<0.0001	1.02 (1.01, 1.03)	<0.0001
Sex						
<i>Female</i>	1	–	1	–	1	–
<i>Male</i>	1.16 (0.84, 1.60)	0.37	1.23 (0.90, 1.67)	0.19	1.17 (0.88, 1.56)	0.29
Access type at first dialysis						
<i>AVF</i>	1	–	1	–	–	–
<i>AVG</i>	1.46 (0.42, 5.09)	0.55	1.19 (0.37, 3.80)	0.77	–	–
<i>Catheter</i>	1.84 (0.97, 3.48)	0.06	1.62 (0.90, 2.90)	0.11	–	–
<i>PD</i>	0.42 (0.03, 5.03)	0.49	0.61 (0.06, 6.29)	0.68	–	–
Access type during follow-up						
<i>AVF</i>	1	–	–	–	1	–
<i>AVG</i>	1.23 (0.27, 5.55)	0.78	–	–	0.77 (0.18, 3.27)	0.72
<i>Catheter</i>	2.93 (1.36, 6.33)	0.006	–	–	2.55 (1.26, 4.97)	0.009
Causes of renal disease						
<i>Hypertension</i>	1	–	1	–	1	–
<i>Glomerulonephritis</i>	2.04 (0.96, 4.36)	0.6	2.20 (1.09, 4.44)	0.03	2.28 (1.14, 4.55)	0.02
<i>Diabetes</i>	2.50 (1.75, 3.58)	<0.0001	2 (1.38, 2.88)	<0.0001	1.84 (1.29, 2.63)	0.001
<i>Other</i>	0.95 (0.61-1.49)	0.84	1.04 (0.66-1.65)	0.85	1.05 (0.68-1.62)	0.81

IRR= incidence rate ratio, AVF= arteriovenous fistula, AVG= arteriovenous graft, PD= peritoneal dialysis

* adjusted for age, sex, access type at start of dialysis, and cause of renal disease

** adjusted for age, sex, access type during follow-up, and cause of renal disease

Discussion

This study gives an overview of the primary reasons and indications for hospitalisation among ESRD patients on haemodialysis in one of the most active MOH hospitals in Makkah City in the western region in Saudi Arabia, which may reflect the severity of patients' co-morbid conditions or the quality of renal care practices. This study highlights the most common causes of hospitalisation among haemodialysis patients, which were genitourinary diseases (35.7-44.6%), cardiovascular diseases (19-26.6%), vascular access (16.1-23.4%), infectious diseases (6.6-12%), and endocrine and metabolic diseases (5.2-10.1%). The length of stay in hospital usually represents the severity of illness and underlying patient health status. This study shows that cardiovascular diseases had the highest impact on an increase in the number of hospital bed days per patient-year on dialysis by 70% compared to other reasons for hospital admission.

Cardiovascular disease is uniquely different in patients with ESRD from those in the general population with earlier onset in life (236, 239-245). Several studies have suggested that the annual rate of hospitalisation and mortality due to cardiovascular disease among patients with ESRD is substantially higher than in general population (159, 212, 235). This study found that cardiovascular disease was the most common reason for hospitalisation, particularly coronary artery disease, which is similar to the general population in Saudi Arabia (246). This may be the result of an increase in the prevalence of coronary artery disease risk factors in the Saudi population such as smoking (247), obesity, metabolic syndrome, diabetes, and hypertension with poor management of chronic diseases or undiagnosed cases (49, 121, 122, 171, 248). These risk factors are strongly associated with an increased risk of developing cardiovascular disease, which may often occur before ESRD (239, 249). Furthermore, this study found that an increase in one year of a patient's age, which is an un-modifiable risk factor, had a significant effect in increasing the length of stay in hospital and the rate of admissions by 2% per patient-year on haemodialysis. Diabetes as a cause of renal disease, and using a catheter as access point for haemodialysis also had a significant effect on the increasing rate of admissions.

In this study, only 7% of haemodialysis patients commenced dialysis with AVF, while the NKF/KDOQI and the Renal Association guidelines for vascular access have recommended that 65% of all incident haemodialysis patients should initiate dialysis with AVF (183, 250).

Although the vast majority of the study population commenced haemodialysis with a catheter as a result of late referral to nephrology care, most of them had converted throughout dialysis time to AVF which is considered as a modifiable risk factor for reducing vascular access complications, especially catheter related infection, and lowering the risk of hospitalisation, as this study demonstrated that patients who had used a catheter throughout the follow-up period showed a 2.5-fold increase in the rate of hospital admissions compared to those who had used AVF. Therefore, the high prevalence of hospital admissions due to vascular access throughout haemodialysis was attributed to creating AVF as a permanent vascular access rather than vascular access complications which also contributed to an increase in hospital utilisation and the cost of haemodialysis care.

The findings of this study demonstrate that the goals of vascular access placement for the NKF/KDOQI and The Renal Association guidelines (183, 250) have been achieved in AKC, whereas the prevalent functional AVF placement rate was around 95% of patients in AKC in 2011, which is higher than the recommended goal of over 65% in NKF KDOQI and 85% in the Renal Association. However, according to the Saudi Centre for Organ Transplantation data report in 2011, the prevalent functional AVF placement rate in all centres in Saudi Arabia was 71% of patients (60), which is lower than the rate in AKC. This indicates the differences in haemodialysis practices and outcomes between healthcare centres. This in turn implies the diversity and cultural competence training in healthcare institutions, or the inequality in allocating healthcare resources between healthcare centres in Saudi Arabia, particularly healthcare providers specialist in nephrology care (27).

Limitations

The potential limitations of this study were that the study was conducted retrospectively for prevalent patients in 2011 due to three main reasons: time limitations for collecting data, a lack of national health information systems in Saudi Arabia, and because some patients were not receiving healthcare in one hospital during the follow-up period of the study. Therefore, it was not possible to examine the trend in the annual rate of hospitalisation for all causes of hospital admission and look at whether there was any significant change in the rate, which might indicate a change in the quality of delivering healthcare services in recent decades. Also, a large amount of critical data for many patients were missing, such as clinical and laboratory measurements at start of dialysis, and the time at which all co-morbid conditions

were diagnosed. Besides, around one-third of the study sample did not have any reported hospitalisation in Al Noor Specialist Hospital. Those patients may have come to the AKC for dialysis sessions as outpatients and may have been hospitalised in another hospital such as a private hospital for inpatient care, or their health conditions may have been good and may not have required hospitalisation. Also, some patients in the study sample who reported admissions might also had undergone admissions in other hospitals. These issues could affect the imprecision of the results. Furthermore, in hospital admissions data records, some patients' diagnoses and procedures may have been incorrectly reported or coded. In addition, the IRR of the admission or length of stay in hospital might not reflect patients' health conditions due to inappropriate hospitalisation in the governmental hospitals in Saudi Arabia. Notably, a survey based on physicians' perspectives highlighted that inappropriate hospitalisation occurred mostly because there was nobody able to look after the patients outside the hospital (251). This is particularly true for elderly patients who require more care than younger patients, as demonstrated in this study by the strong association of the rate of length of stay in hospital and the rate of admissions with increasing patient age. Inappropriate hospitalisation might not be the reason for the increase in the rate of length of stay in hospital or admissions among haemodialysis patients in this study population. An increase in the rate of length of stay in hospital in this study might really reflect the severity of patients' co-morbid conditions disease especially among elderly patients as a result of rapid progression of chronic diseases and their complications.

Strengths

This study reveals that the most frequent reasons for hospital admission among haemodialysis patients were cardiovascular disease particularly hypertension and coronary artery disease, vascular access due to creating AVF after starting dialysis, infectious diseases particularly respiratory infectious disease, and endocrine and metabolic disorders. Increased age, diabetes as a cause of renal disease, and using a catheter as access point for haemodialysis have a significant effect in increase the rate for hospital admissions per patient-year on haemodialysis. These indications for hospital admissions provide evidence for public health administrators and healthcare providers in Saudi Arabia to develop multidisciplinary strategies for improving pre-ESRD nephrology care practice, and the quality of healthcare management for multiple chronic diseases and their complications, patients'

health behaviours and awareness about their illness. These strategies would be valuable in the future to improve healthcare outcomes and reduce hospital utilization and the cost of haemodialysis care. Furthermore, this study suggests that health information systems must be developed in Saudi Arabia to allow further research to be conducted to review regularly the quality of haemodialysis cares and outcomes in all MOH and non-MOH centres. More indications for hospitalisation and consequences of practices related to hospitalisation for haemodialysis patients should be studied to provide a comprehensive evidence-based health policy for haemodialysis patients in Saudi Arabia.

Conclusion

This study describes all of the relevant literature related to the aetiology of renal disease in Saudi Arabia. The findings of this study are that diabetes and hypertension are the most prevalent causes of ESRD, and that increased age and diabetes as a cause of ESRD has a significant contribution in the increased rate of hospital admissions among haemodialysis patients. Thus cardiovascular disease was the most common reason for hospital admission, and had a significant impact to increase the length of stay in hospital with increasing age. Furthermore, pre ESRD nephrology care practice should be improved to reduce or eliminate initiating dialysis with catheter which associate with increase the rate of hospital admission among haemodialysis patients. Health information systems must be developed in Saudi Arabia to allow further researches to be conducted to investigate other indications for hospitalisation such as clinical and laboratory measurements, and healthcare providers specialist services; and consequences of practices related to hospitalisation for haemodialysis patients to provide a comprehensive evidence-based health policy for haemodialysis patients in Saudi Arabia.

CHAPTER 6

Conclusions and recommendations

With limited healthcare resources, the pattern of disease has changed in Saudi Arabia in recent decades from communicable to non-communicable diseases (4) as a result of the rapid economic growth that is contributing to increased health risk behaviours in Saudi Arabia, including lack of physical activity, poor nutrition, and smoking (49, 247, 252-255). These are responsible for much of the illness, suffering, and early deaths related to chronic diseases in Saudi Arabia (256). Many reports in the literature have shown that the prevalence of obesity (26, 49), diabetes mellitus (122, 125), and cardiovascular disease (121, 257) are high in the Saudi population. All these are risk factors for developing chronic kidney disease (CKD) besides a family history of CKD and increased age. Chronic kidney disease is becoming a worldwide public health problem as it is linked with an increase in the incidence and prevalence rate of patients with renal failure who require renal replacement therapy with high healthcare costs and poor outcomes. Moreover, CKD in its earlier stages is associated with a higher prevalence of many adverse outcomes such as renal failure, cardiovascular disease, and premature death (258). Therefore, more attention to the prevention and management of CKD is required in Saudi Arabia.

Poor management of diabetes and hypertension increases the risk of progression of CKD to end-stage renal failure. Also, infections, and conflicts in prescribing medications (259, 260) or toxins injurious to the kidney can contribute to progression of CKD to end-stage renal failure particularly in the elderly people in Saudi Arabia. The incidence rate of end-stage renal disease (ESRD) has increased substantially in Saudi Arabia with a large proportion of incidence and prevalence of ESRD found among middle-aged patients, while the proportion of males is slightly higher than females but there was no significant difference between them. The predominant causes of ESRD in Saudi Arabia are diabetes and hypertension. The prevalence

of diabetic nephropathy as a cause of ESRD has increased significantly in all regions of Saudi Arabia in the past two decades, while the trend of hypertensive nephropathy has not changed, and with the changing patterns of disease the prevalence of glomerulonephritis as a cause of ESRD has decreased remarkably. This means that diabetes has a significant contribution in increasing the risk of ESRD in Saudi Arabia.

Furthermore, the majority of patients with CKD who progressed to ESRD were referred from an emergency department for urgent dialysis in two of the most active Ministry of Health (MOH) hospitals in the western region of Saudi Arabia. This implies that patients, who are diabetic or hypertensive during middle-age, and at high risk for progression of CKD were not detected in the general population, or they were diagnosed but were not followed up consistently, or they were not educated efficiently about their illness and its potential complications. This reveals the current status of chronic diseases management, including CKD in Saudi Arabia, and emphasises the importance of developing multidisciplinary preventive strategies to prevent or delay the progression of renal disease, and reduce the incidence rate of ESRD and its complications, and related healthcare cost. The National Kidney Foundation – Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) guidelines states that adverse outcomes of CKD, such as loss of kidney function, kidney failure, and cardiovascular disease, can be prevented or delayed by detecting and treating CKD at earlier stages (185).

This strategy includes consistently first detecting and screening people at high risk of CKD who are often diabetic or hypertensive in the Saudi population. The NHS Health Check Programme for adults in England may be a model that could be considered in Saudi Arabia to help achieve this objective (261). Second, improving the rate of early referral of patients with CKD to nephrology care; this will be achieved by increasing the awareness of other healthcare professionals, including primary care physicians, cardiologists, diabetologists, and internists about the importance of early diagnosis and effective treatment measures of CKD. Also, encouraging communication between healthcare practitioners, and closer collaboration between primary and secondary healthcare professionals in all healthcare sectors in Saudi Arabia to provide optimal renal care, which includes creating guidelines for other healthcare professionals that clarify the criteria of when the patient with CKD should be referred to nephrology care, and educate patients about their illness and train them for self-management. Improving the rate of early referral to nephrology care for patients with CKD

also give patients who are expected to progress to ESRD the chance to consider and decide between renal replacement therapy (RRT) options. This will help to improve pre-emptive renal transplantation, and allow time to create arteriovenous fistula as a permanent vascular access point for dialysis, which is considered a modifiable risk factor for vascular access complications; thus the hospital utilisation and healthcare cost will be reduced.

Investigating morbidity conditions among patients with ESRD in Saudi Arabia revealed that the highest prevalence morbidity conditions were hypertension and Hepatitis C Virus (HCV) infection. Although the prevalence of HCV has apparently declined in recent decades among patients with ESRD in Saudi Arabia, there are many factors contributing to the high prevalence of HCV particularly among haemodialysis patients. These factors include the effects of nurse understaffing, which means that the staff were not highly trained overall. Other factors may increase the risk of HCV, such as the length of dialysis, or the number of blood transfusions that might have involved incomplete or absent anti-HCV screening of donated blood. The relations between all these factors and the high prevalence of HCV, which is associated with a high rate of chronic liver disease and cirrhosis, among haemodialysis patients should be investigated in a prospective longitudinal study to provide a comprehensive evidence-based health policy.

Cardiovascular disease was the leading cause of hospitalisation and mortality among patients with ESRD in Saudi Arabia. Investigating the indications for hospitalisation, which usually reflect either the quality of healthcare services, or the severity of patients' co-morbid conditions, among haemodialysis patients in one of the most active MOH hospitals in Makkah City in the western regions of Saudi Arabia has revealed that diabetes and hypertension are the most common causes of ESRD, and that increased age and diabetes as a cause of ESRD has a significant contribution in the increased rate of hospital admissions among haemodialysis patients. Thus cardiovascular disease was the most common reason for hospital admission, and had a significant impact to increase the length of stay in hospital with increasing age. However, CKD is an important risk factor for cardiovascular disease even before progressing to ESRD and onset RRT, while other risk factors for cardiovascular disease that require careful attention in people with CKD include smoking tobacco and water pipes, uncontrolled high blood pressure, elevated blood sugar, excessive weight, and elevated cholesterol (262). Further studies are needed to investigate more indications for

hospitalisation among patients with ESRD in Saudi Arabia to assess the effect of pre-ESRD care practice, clinical and laboratory measurement at onset of ESRD, and the specialised healthcare providers; to provide evidence based-health policy to improve the quality of healthcare management for those individuals at high risk of CKD in Saudi population, and reduce the cost of healthcare.

The national health information system must be developed in Saudi Arabia to provide comprehensive data on the health of the populations and its use of health services. Also, healthcare practitioners should be trained on how to report and code the diagnosis and healthcare procedures correctly. This will play the main role in developing the preventive strategy of CKD and its risk factors, and improve the communication between healthcare providers to implement the best healthcare practice, which would help in reducing medical errors and duplications of healthcare services. Also, it will help in conducting further studies for assessing the overall quality of renal care regularly to provide an updated evidence-based health policy. The further studies should be concern with:

- Assessing and describing the epidemiology of CKD and ESRD to improve the quality of healthcare management. For instance, tracking the trend of the incidence rate of ESRD among diabetic or hypertensive patients. Also, a longitudinal study is required to investigate the reason for the high prevalence of HCV among haemodialysis patients.
- Evaluating pre-ESRD care practice and its outcomes in order to implement the best intervention that will help to improve pre-ESRD care practice outcomes in Saudi Arabia. Particularly, the best time of referring patients with CKD to nephrology care should be investigated.
- Investigating other indications for hospitalisation such as clinical and laboratory measurements, healthcare providers specialist services, and consequences of healthcare practices that related to hospitalisation among haemodialysis patients.

In summary, this thesis presents an evidence of the increasing burden of ESRD in Saudi Arabia. It stressed the needs and the importance of multidisciplinary preventive strategies for leading causes of ESRD, which are diabetes and hypertension. Also, it provides an evidence for the need of improving pre-ESRD nephrology care practice and the collaboration between healthcare providers. Furthermore, it highlights the need for a comprehensive national health

information system to allow regular screening for those people at high risk and to detect CKD in the early stages and to describe the epidemiological pattern of ESRD in Saudi Arabia. This would allow the identification of priority areas for further research to assess the quality of healthcare management and provide an updated evidence-based health policy that will help healthcare providers to choose the best intervention that will help to improve healthcare practice outcomes for patients with CKD and allocate healthcare resources appropriately.

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Appendices

Appendix A - Search strategy

- 1** ((end stage or terminal or chronic) adj3 (renal* or kidney*)).mp. [mp=ab, sh, hw, ti, tn, ot, dm, mf, nm, ui, an]
- 2** ((Saudi or emirates or Kuwait or Oman or Bahrain or Qatar) adj5 (middle east* or Arab*)).mp. [mp=ab, sh, hw, ti, tn, ot, dm, mf, nm, ui, an]
- 3** 1 and 2

Appendix B - Data extraction form

Page 1

Data Extraction Form for a systematic review of the epidemiology of end-stage renal disease in the countries of the Gulf Cooperation Council

Reviewer initial:

Study ID: (Author: Year)

Description of the study

Study design	Cohort Cross-sectional	Case-control Ecological Study
The objective of the study	Incidence Prevalence Mortality rate Causes of Mortality Primary causes co-morbidities Co-morbid conditions	
Validation of ESRD	Biochemical or medical record	Self-report
Renal replacement modalities	Renal Transplantation [%] Dialysis (Haemodialysis [%] – Peritoneal dialysis [%])	
Study setting	Country: How many centres: Population size: Age: Sex: Male [%] Female [%] Duration of dialysis:	

Participants

Inclusion criteria			
Exclusion criteria			
Participants studied	Disease	No disease	Notes
Number enrolled into study			
Number lost to follow up			
Final number of participants evaluated			

Assessing the methodological quality of the study

Newcastle – Ottawa Scale	Case-control studies & Cross-sectional studies		Cohort studies	
1. Selection	Case definition Representativeness of cases Selection of control Definition of controls		Representativeness of exposed cohort Selection of non exposed cohort Ascertainment of exposure Outcome occurred	
2. Comparability	Matching / adjustment for age Matching / adjustment for other factors Factors=.....		Matching / adjustment for age Matching / adjustment for other factors Factors=.....	
3. Ascertainment	Ascertainment of exposure Same method of ascertainment for cases and controls Non response rate		Ascertainment of outcome Was follow up long enough for outcomes to occur Adequacy of follow up of cohort	
Score:				

Data Extraction Form for a systematic review of the epidemiology of end-stage renal disease in the countries of the Gulf Cooperation Council

Reviewer initial:

Study ID: (Author: Year)

Primary outcome measures

1- End-stage Renal Disease ☐ Prevalence rate ☐ Incidence rate ☐ Mortality rate 2- ☐ Primary causes 3- ☐ Co-morbid conditions 4- ☐ Mortality causes
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Results

Primary Outcomes	Group, N=	Group, N=	Group, N=

Additional notes

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Appendix C - Causes of hospitalization

Non-infectious diseases

Anaemia

- D50 Iron deficiency anemia
- D59 Acquired hemolytic anemia
- D63 Anemia in other chronic diseases classified elsewhere
- D64 Other anemias
- D69 Purpura and other hemorrhagic conditions

Diseases of the musculoskeletal system

- M84 Disorder of continuity of bone
- M90 Osteopathies in diseases classified elsewhere
- M96 Intraoperative and postprocedural complications and disorders of musculoskeletal system, not elsewhere classified

Diseases of the digestive system

- K21 Gastro-esophageal reflux disease
- K25 Gastric ulcer
- K29 Gastritis and duodenitis
- K35 Acute appendicitis
- K40 Inguinal hernia
- K42 Umbilical hernia
- K57 Diverticular disease of intestine
- K59 Other functional intestinal disorders
- K60 Fissure and fistula of anal and rectal regions
- K61 Abscess of anal and rectal regions
- K62 Other diseases of anus and rectum,subcoding
- K74 Fibrosis and cirrhosis of liver
- K76 Other diseases of liver
- K80 Cholelithiasis
- K81 Cholecystitis
- K85 Acute pancreatitis
- K92 Other diseases of digestive system
- R10 Abdominal and pelvic pain
- R18 Ascites
- R19 Other symptoms and signs involving the digestive system and abdomen
- R19 Other symptoms and signs involving the digestive system and abdomen

Disease of the nerve system

- G40 Epilepsy and recurrent seizures
- G56 Mononeuropathies of upper limb
- G81 Hemiplegia and hemiparesis

- R52 Pain, unspecified
- R56 Convulsions, not elsewhere classified

Diseases of the respiratory system

- J45 Asthma
- J81 Pulmonary oedema
- J86 Pyothorax
- J90 Pleural effusion, not elsewhere classified
- J93 Pneumothorax and air leak
- R04 Hemorrhage from respiratory passages
- R09 Other symptoms and signs involving the circulatory and respiratory system

Diseases of the genitourinary system

- N05 Unspecified nephritic syndrome
- N13 Obstructive and reflux uropathy
- N18 Chronic kidney disease
- N20 Calculus of kidney and ureter
- N21 Calculus of lower urinary tract
- N23 Unspecified renal colic
- N25 Disorders resulting from impaired renal tubular function
- N39 Other disorders of urinary system
- N40 Enlarged prostate
- N93 Other abnormal uterine and vaginal bleeding
- Q61 Cystic kidney disease
- Q64 Other congenital malformations of urinary system
- Q87 Other specified congenital malformation syndromes affecting multiple systems
- R33 Retention of urine
- R87 Abnormal findings in specimens from female genital organs
- Z49 Encounter for care involving renal dialysis
- Z94 Transplanted organ and tissue status

Diseases of the circulatory system

- I10 Essential (primary) hypertension
- I11 Hypertensive heart disease
- I12 Hypertensive chronic kidney disease
- I21 ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
- I24 Other acute ischemic heart diseases
- I25 Chronic ischemic heart disease
- I30 Acute pericarditis
- I31 Other diseases of pericardium
- I42 Cardiomyopathy
- I44 Atrioventricular and left bundle-branch block
- I47 Paroxysmal tachycardia
- I48 Atrial fibrillation and flutter

- I50 Heart failure
- I60 Nontraumatic subarachnoid hemorrhage
- I63 Cerebral infarction
- I67 Other cerebrovascular diseases
- I70 Atherosclerosis
- I74 Arterial embolism and thrombosis
- I82 Other venous embolism and thrombosis
- I95 Hypotension
- I96 Gangrene, not elsewhere classified
- I97 Intraoperative and postprocedural complications and disorders of circulatory system, not elsewhere classified
- O10 Pre-existing hypertension complicating pregnancy, childbirth and the puerperium
- R00 Abnormalities of heart beat

Disease of the skin

- L98 Other disorders of skin and subcutaneous tissue, not elsewhere classified

Endocrine and metabolic diseases

- E08 Diabetes mellitus due to underlying condition
- E16 Other disorders of pancreatic internal secretion
- E21 Hyperparathyroidism and other disorders of parathyroid gland
- E83 Disorders of mineral metabolism
- E87 Other disorders of fluid, electrolyte and acid-base balance

Miscellaneous

- O14 Pre-eclampsia
- Z93 Artificial opening status
- Z98 Other postprocedural states

Trauma or injury related condition

- S31 Open wound of abdomen, lower back, pelvis and external genitals
- T14 Injury of unspecified body region
- T86 Complications of transplanted organs and tissue
- T81 Complications of procedures, not elsewhere classified

Vascular access [creation, problem]

- T80 Complications following infusion, transfusion and therapeutic injection
- T81 Complications of procedures, not elsewhere classified
- T82 Complications of cardiac and vascular prosthetic devices, implants and grafts
- Z49 Encounter for care involving renal dialysis

Infectious disease

Sepsis

- A41 Other sepsis

Infections of the skin and subcutaneous tissue

- L02 Cutaneous abscess, furuncle and carbuncle
- L03 Cellulitis and acute lymphangitis
- L04 Acute lymphadenitis

Infectious arthropathies

- M00 Pyogenic arthritis

Intestinal infectious diseases

- A09 Infectious gastroenteritis and colitis, unspecified

Respiratory infectious diseases

- A15 Respiratory tuberculosis
- A19 Miliary tuberculosis
- J02 Acute pharyngitis
- J18 Pneumonia, unspecified organism
- J20 Acute bronchitis
- J69 Pneumonitis due to solids and liquids

Viral infection

- B17 Other acute viral hepatitis
- B34 Viral infection of unspecified site
- Other infectious diseases
- H60 Otitis externa

Publications

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

PAPER



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

Amal A. Hassanien¹ • Fahdah Al-Shaikh² • Eszter P. Vamos³ • Ghasem Yadegarfar⁴ • Azeem Majeed⁵

¹Department of Primary Care & Public Health, School of Public Health, Imperial College London, UK

²School of Public Health, Imperial College London, UK

³Department of Primary Care & Public Health, School of Public Health, Imperial College London, UK

⁴Research Design Service London and Department of Primary Care & Public Health, School of Public Health, Imperial College London, UK

⁵Professor of Primary Care and Head of the Department of Primary Care & Public Health, School of Public Health, Imperial College London, UK

Correspondence to: Amal A. Hassanien. Email: a.hassanien09@imperial.ac.uk

DECLARATIONS

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None declared

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AH designed and coordinated the study, conducted a systematic review and statistical analysis; and drafted the manuscript. AM contributed to the design and coordination of the study and reviewed the manuscript EV

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

contributed to the design of the study and reviewed the manuscript GY contributed to statistical analysis, and reviewed the manuscript FA conducted a systematic review and reviewed the manuscript

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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.

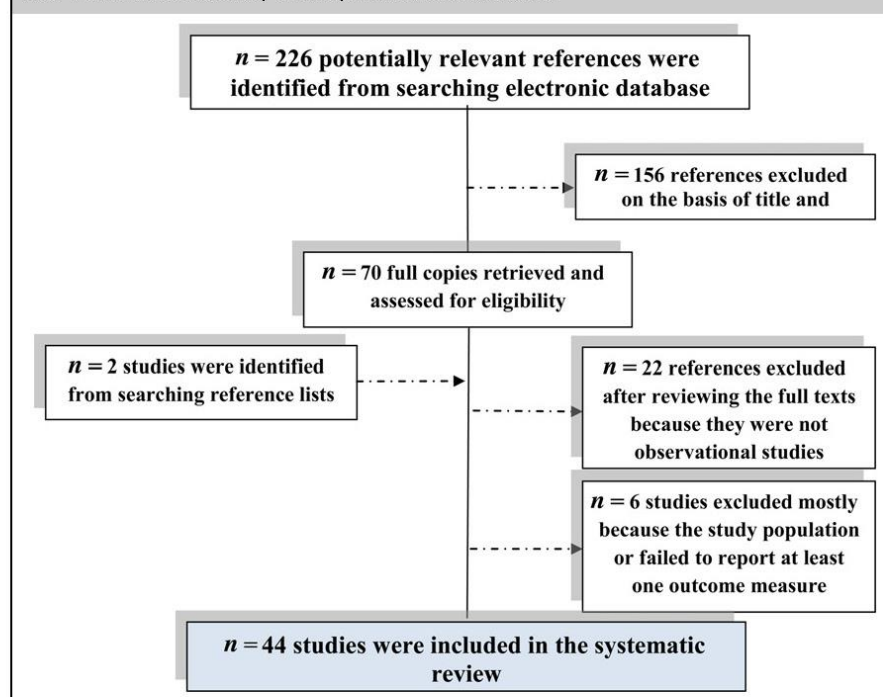
Studies that met the inclusion criteria for the review had data extracted. Data relating to study design, setting, definition of outcomes measure, inclusion and exclusion criteria of study population, methodological quality using the Newcastle Ottawa Scale (NOS)¹⁷ and outcomes were then independently 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). Sub-group 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

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 polymorphism 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 dialysis maintenance	Cohort	KSA/West-Talef	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 range	Age range	Male %	RRT			ESRD patients
										HD%	PD%	RT%	
50	Younbissi	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-Hafuf	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 septicemia among patients on haemodialysis in Al-Hasa region of Saudi Arabia	Cohort	KSA/East-Hafuf	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

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-Haifouf	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 unit	Cohort	KSA/East-Haifouf	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-Haifouf	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 range	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 cyclor machine	Cross-sectional	KSA/West-Talef	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-Talef	4	43	6–89	53.84	63.8	1.2	35	325
37	Hurait	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-Gassim	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, Gaizan = 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 troponin 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	Cross-sectional	KSA/East-Dammam	3	38	21-75	39	100	-	-	256
33	Al-Suwaid	2007	The Gulf survey on haemodialysis 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 Macro-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

Bahrain²⁵ 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 1994²⁴ 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 uremic 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/Pylonephritis 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 medullary 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 embolism), 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 Giza 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 infection⁴³ 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 septicemia.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 comorbidities 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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Review of pre end-stage renal disease care in the western region in Saudi Arabia

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Review of pre end-stage renal disease care in the western region in Saudi Arabia

Amal A Hassanien^{1*}, Azeem Majeed¹, Hilary Watt¹ and Nawal Basri²

*Correspondence: a.hassanien09@imperial.ac.uk

¹Department of Primary Care & Public Health, School of Public Health, Imperial College London, UK.

²Jeddah Kidney Centre, King Fahad General Hospital in Jeddah, Ministry of Health in Saudi Arabia, KSA.

Abstract

Background: The risk factors for chronic kidney disease (CKD) are increasing in the Saudi population. Consequently, the incidence and prevalence of end-stage renal disease (ESRD) have increased substantially in Saudi Arabia over the past three decades. This study was conducted to review pre-ESRD care and investigate the primary causes of ESRD among haemodialysis patients in the western region in Saudi Arabia.

Methods: A pilot cross-sectional study was conducted in Al-Noor Kidney Centre and Jeddah Kidney Centre in the western region of Saudi Arabia. Participants were patients with ESRD on regular haemodialysis during 2011. Main outcome measures were pre-ESRD care including: reason of referral to nephrology care, source of referral to nephrology care, duration of pre-ESRD care, and vascular access at the first dialysis; and primary causes of ESRD.

Results: Preliminary indicators of pre-ESRD care showed that: endocrine, nutritional and metabolic diseases, and immunity disorders were the principal reason for patient referral in 50.6% (95% CIs, 45.1_56.1) of patients; 50.6% (95% CIs, 45.6_55.6) of the patient referrals arrived from the emergency department; a large proportion of haemodialysis patients were not receiving pre-ESRD nephrology care, 47.6% (95% CIs, 41.7_53.5); the predominant vascular access point for haemodialysis was initially a catheter 88.3% (95% CIs, 84.5_91.3). The dominant causes of ESRD were hypertensive nephropathy, 55.8% (95% CIs, 50.8_60.7) and diabetic nephropathy, 24.6% (95% CIs, 20.4_29.1).

Conclusions: Pre-ESRD nephrology care needs to be improved in Saudi Arabia. Potential strategies could involve: regular screening of high risk people, encouraging communication between healthcare practitioners, and education on the need to refer patients with CKD to nephrology care in earlier disease stages; and increasing patients' awareness about their health conditions and potential consequences of their kidney disease.

Keywords: Chronic kidney disease, end-stage renal disease, nephrology care

Background

End-stage renal disease (ESRD) has emerged as an important public health issue worldwide, because of the marked increase in its incidence and prevalence. This increases the need for multidisciplinary management including financial and social support, and medical care. Early referral of patients with chronic kidney disease (CKD) to specialized renal services can help to preserve renal function and delay the progression of renal failure by preventing and managing the modifiable risk factors of CKD and treating secondary complications [1-3].

Many studies have shown that a long duration of pre-ESRD nephrology care, which is the period between the first time the patient has been seen by a nephrologist and the first dialysis [1], has a significant effect on the quality of life and survival rate in patients with ESRD before and after receiving renal replacement therapy (RRT) [2,4,5]. Improved detection of patients with CKD in its early stages can significantly reduce the prevalence of cardiovascular morbidity, and gives an adequate time to prepare patients for RRT; especially those patients who need to create vascular access for dialysis, as maturation of arterio-venous fistula (AVF) takes from 6 to 8 weeks; and helps to improve pre-emptive renal transplantation treatment [1,3].

National Kidney Foundation- Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) guidelines recommended that the preparation for RRT should start in CKD stage 4, when the estimated Glomerular Filtration Rate (eGFR) is <30 ml/min/1.73m² [1]. This gives time to choose and create a suitable dialysis access point, considered a modifiable risk factor for bacteraemia and mortality [6,7], and avoids the need for temporary vascular access. These interventions have a significant impact in improving the quality of life and reducing the financial demands of renal care.

Many reports have shown evidence of increasing prevalence of the most common causes of ESRD in Saudi Arabia such as diabetes [8], and obesity- conditions associated with many chronic diseases [9-11]. Furthermore, the incidence and prevalence of RRT have been increasing substantially in the last three decades [12]. The majority of patients with ESRD are getting their RRT in the form of haemodialysis (around 53.7%), with 5.1% on peritoneal dialysis, and with 41.2% renal graft. Around 70% of RRT is provided by Ministry of Health free of charge [13].

This study was conducted to review pre-ESRD care and to investigate primary causes of ESRD among haemodialysis

patients in the western region of Saudi Arabia. Pre-ESRD nephrology care was reviewed by describing the preliminary indicators including: the reason of referral to nephrology care, referral source to nephrology care, pre-ESRD care period, and access type at the first dialysis. The results of this study may be valuable for public health planners and healthcare professionals in Saudi Arabia to prepare a strategy to define and screen people at high risk and improve rates of early referral to nephrology care, both which rely upon multidisciplinary demands.

Methods

Study design and setting

A cross-sectional study was conducted in two large haemodialysis centers in the western region of Saudi Arabia: Alnoor Kidney Centre (AKC) in Al Noor Specialist Hospital in Makkah city and Jeddah Kidney Centre (JKC) in King Fahad General Hospital in Jeddah city. Both are Ministry of Health Hospitals, and therefore are expected to have similar quality of healthcare services. Data was obtained after applying for ethical approval from the Ministry of Health & General Directorate of Health Affairs in each city.

Study population

Participants were the prevalent patients with ESRD on regular haemodialysis during 2011. This haemodialysis population was chosen for two reasons: according to Saudi Centre for Organ Transplantation report, they constitute the largest population among patients with RRT in Saudi Arabia [14], these patients are easy to find, extract their medical history, and follow-up retrospectively from medical records in dialysis centers despite the lack of primary care networks and health information systems. All visiting patients to dialysis centers, who do not have a documented medical history in medical records, and patients with advanced malignancy were excluded.

Data collection

Electronic medical records were searched to identify all patients with ESRD on haemodialysis in 2011. The total number of patients on haemodialysis in Al-Noor Specialist Hospital in Makkah was 418, and King Fahad General Hospital in Jeddah was 634. A simple random sampling technique was used to select a sample of 69 patients from JKC because of time limitations; all patients from AKC were included except 84 visiting patients to the dialysis centre without a medical history who were excluded. The requested data including demographic information, date first seen by nephrologist, reason of referral to nephrologist, referral source to nephrology care, date of first dialysis, access type at first dialysis, and causes of ESRD were collected from medical records and stored in a customized Microsoft Office Access database.

Statistical analysis

Patient's age at referral time to nephrology care and the pre-ESRD care period were calculated. Pre-ESRD care period

was categorized as following: 0 months, <6 months, 6-12 months, and >12 months. Reasons of referral to nephrologists were classified using ICD-9-CM: disease of the genitourinary system including disorders of urethra and urinary tract such as haematuria; disease of the circulatory system including uncontrolled blood pressure; endocrine, nutritional and metabolic diseases and, immunity disorders including diabetic nephropathy, nephrolithiasis, disorders of fluid electrolyte such as hyperkalaemia and hyperphosphatemia, and unspecified disorders of metabolism; symptoms and signs indicate to renal diseases including proteinuria, abnormal creatinine clearance, and eGFR <30; and not reported. Also, primary causes of ESRD were classified according to ICD-9-CM to the following categories: diabetes, glomerulonephritis (GN), secondary GN/vasculitis, interstitial nephritis/pyelonephritis, hypertension/large vessel disease, cystic/hereditary/congenital diseases, neoplasms/tumors, and miscellaneous conditions.

Data were analyzed descriptively to describe the preliminary indicators of pre-ESRD care and investigate the primary causes of ESRD. To examine uncertainty, the 95% confidence intervals (CIs) were calculated for each outcome. Additional analyses were also performed. T-test for two independent means was performed to examine the associations between age at referral time to nephrology care and sex. Chi-square or Fisher exact test was performed to examine the relation between the pre-ESRD care period with age, sex, referral source, the reason of referral to nephrology care, dominant causes of ESRD, and AVF as vascular access at first haemodialysis. Logistic regression was performed to examine the association between AVF as vascular access at first haemodialysis with age, sex, referral source, the reason of referral to nephrology care, period of pre-ESRD, and dominant causes of ESRD as predictors. All the analyses were performed using STATA 11.

Results

Patients' characteristics

The total sample size was 403 haemodialysis patients, derived from two dialysis centers: 334 from AKC and 69 from JKC (Figure 1). 93.1% of the study population were Saudis. Males constituted 57.3 % of the study population. The mean age at referral time to nephrology care was 44.3 (standard deviation (SD) = ± 16.4). T-test shows that there was no significant difference between the mean age for males (43.6) and females (45.4) at referral time to nephrology care with a mean difference of (1.8; 95% CIs, -2.01 to 5.8; $p=0.18$). The mean of period of haemodialysis was 6.2 years ($SD=\pm 5.2$). 27 patients of the study sample died, and 10 had renal transplantation during 2011 in AKC (Table 1).

Preliminary indicators of pre-ESRD care and primary causes of ESRD

In the study sample, the most commonly reported reasons for referral to nephrology care are endocrine, nutritional and metabolic diseases, 50.6%, followed by disease of circulatory system, 39.9%, symptoms and signs indicate to renal function

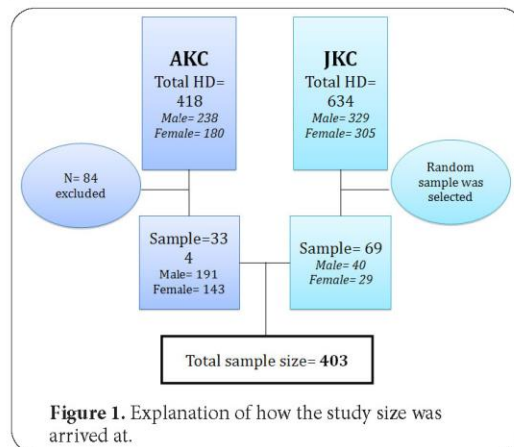
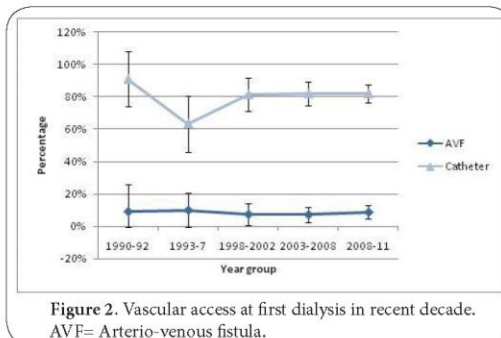


Table 1. Summary of Patients characteristics.

Patient characteristics	Outcome
Patients' source	
Alnoor Kidney Centre	334
Jeddah Kidney Centre	69
Age at referral to nephrology care	
Mean(SD)	44.3(16.4)
Range(low, high)	(1.9, 89.7)
Missing	113
Sex (%)	
Male	231(57.3)
Nationality (%)	
Saudi	375(93.1)
Period of dialysis in years	
Mean(SD)	6.2(5.2)
Range(low, high)	(0.01, 21.2)
Missing	13
Patient status during 2011	
Survive	366
Dead	27
Renal transplanted	10

SD= standard deviation.

deterioration, 6%, diseases of genitourinary system, 3.6%; in 67 records, reasons for referral were missing or not reported. Referral from the emergency departments for urgent dialysis served as the principal referral source for 50.6%; other sources included from out-patient clinics for renal care, 27.8%, and from different healthcare centers for dialysis, 21.6%. The pre-ESRD care period ranged between 0-274 months with 113 missing records. 47.6% of haemodialysis patients had not



received pre-ESRD nephrology care, 28.6% of patients had received care for <6 months, 6.9 % received care between 6-12 months, and 16.9% received care for >12months. The principal access point for dialysis in the study sample was via a catheter at 88.3%. 8.9% were initiated through an AVF, 2.5% initiated with an arterio-venous graft and 0.3% were initiated with peritoneal dialysis. To avoid misinterpretation, the trend for AVF and catheter as vascular access at first dialysis was examined (Figure 2). There has been no improvement in referring patients to create AVF before first dialysis during the last decade, while the number of patients who started dialysis with catheter has not decreased. The dominant cause of ESRD is hypertension/large vessel disease, 55.8% followed by diabetes, 24.6%, cystic/hereditary/congenital disease, 7.2 %, GN 6.5%, interstitial nephritis or pyelonephritis, 4.5%, secondary GN/vasculitis, 1%, and 0.5% unknown (Table 2).

Comparisons

There was no significant statistical relation between pre-ESRD care period with age ($p=0.06$), sex ($p=0.6$), diabetic nephropathy ($p=0.6$) and hypertensive nephropathy ($p=0.97$) as primary causes of ESRD. The relation between pre-ESRD care period and reason of referral to nephrology care was statistically significant ($p=0.005$), where the majority of patients within all reasons of referral had not received pre-ESRD nephrology care or they had received care but for less than six months. There was a significant association between pre-ESRD care period and referral sources ($p<0.0001$), where patients with CKD who had not received pre-ESRD care were more likely to be referred from emergency departments. Consequently, there is a strong relation between pre-ESRD care periods and initiating haemodialysis with AVF ($p<0.0001$) (Table 3).

The relationship between initiating haemodialysis with AVF with age, and sex were not statistically significant. However, it seems there is a proportional relationship between pre-ESRD care period and initiating haemodialysis with AVF. Patients who had received care for between 6-12 months were less likely by 60% to initiate haemodialysis with AVF (OR=0.4,

Table 2. Preliminary indicators of pre-ESRD care and primary causes of ESRD

Outcome	Frequency	%(95% CIs)
Reason of referral to nephrologist		
Diseases of genitourinary system	12	3.6(1.9_6.2)
Disease of circulatory system	134	39.9(34.6_45.3)
Endocrine, nutritional and metabolic diseases & immunity disorders	170	50.6(45.1_56.1)
Symptoms and signs indicate to renal diseases	20	6(3.7_9.0)
Missing/Not reported	67	-
Referral source		
Emergency	204	50.6(45.6_55.6)
Outpatient clinic	112	27.8(23.5_32.4)
Other healthcare centres	87	21.6(17.7_25.9)
Period of pre-ESRD care/month		
0 months (Not receiving pre-ESRD care)	138	47.6(41.7_53.5)
<6 months	83	28.6(23.5_34.2)
6-12 months	20	6.9(4.3_10.5)
>12 months	49	16.9(12.8_21.7)
Missing/Not reported	113	-
Access at first dialysis		
AVF	32	8.9(6.2_12.4)
AVG	9	2.5(1.2_4.7)
Catheter	317	88.3(84.5_91.3)
PD	1	0.3(0_1.5)
Missing/Not reported	44	-
Primary causes of ESRD		
Cystic/Hereditary/Congenital disease	29	7.2(4.9_10.2)
Diabetes	99	24.6(20.4_29.1)
Glomerulonephritis	26	6.5(4.3_9.3)
Hypertension/Large vessel disease	225	55.8(50.8_60.7)
Interstitial nephritis/Pyelonephritis	18	4.5(2.7_7)
Secondary GN/Vasculitis	4	1(0.3_2.5)
Miscellaneous conditions	2	0.5(0.1_1.8)

AVF= arterio-venous fistula, AVG= arterio-venous graft, PD= peritoneal dialysis.

95% CIs, 0.1 to 1.7; $p=0.2$) but there was insufficient evidence for this association, while patients who had received care for <6 months were less likely by 70% to initiate haemodialysis with AVF (OR=0.3; 95% CIs, 0.14 to 0.9; $p=0.02$) compared to patients who had received care >12 months. Thus, patients who were referred from other different healthcare centers for renal care were two times more likely to initiate haemodialysis with AVF but this association is not statistically significant (OR=2, 95% CIs, 0.6 to 6.6; $p=0.2$), and patients who were referred from outpatients clinics were six times more likely

to initiate haemodialysis with AVF (OR=6.3; 95% CIs, 2.7 to 15.5; $p<0.0001$) compared to patients who were referred from emergency departments. Also, there is a significant association between the reason of referral to nephrology care and initiating haemodialysis with AVF in the study sample. The patients who were referred to nephrology care because of circulatory system diseases were less likely by 80% (OR=0.2; 95% CIs, 0.04 to 0.6; $p=0.005$); and endocrine, nutritional and metabolic diseases were less likely by 9% (OR=0.07; 95% CIs, 0.02 to 0.3; $p<0.0001$) to initiate haemodialysis with AVF compared to patients who were referred because of genitourinary system diseases. Patients with diabetic nephropathy were 46% less likely to initiate haemodialysis with AVF compared to non-diabetic patients (OR=0.54; 95% CIs, 0.2 to 1.4; $p=0.2$); also, patients with hypertensive nephropathy were 62% more likely to initiate haemodialysis with AVF compared to non-hypertensive patients (OR=1.62; 95% CIs, 0.77 to 3.5; $p=0.2$); however, these relationships were not statistically significant (Table 4).

Discussion

In Saudi Arabia, the risk factors for CKD have risen in recent decades with a corresponding rise in the incidence and prevalence of RRT. We reviewed pre-ESRD care and the primary causes of ESRD to provide evidence of the quality of renal care services before starting dialysis.

The indicators of pre-ESRD nephrology care show that; around 41.7-53.5% of haemodialysis patients had not received renal care at all before initiating dialysis, and around 23.5-34.2% had received care but for less than six months. This means there is a reduced chance for patients to take part in clinical decisions regarding RRT options. Also, it means inadequate time to provide a pre-dialysis educational program and psychological preparation for patients with CKD, and inadequate time to create a suitable point for permanent vascular access to be used at first dialysis.

This resulted in around 45.6-55.6% of patients with ESRD being referred from emergency departments for urgent haemodialysis. This in turn led to around 84.5-91.3% of patients with ESRD to have initiated haemodialysis with a catheter, which is associated with increased risk of hospitalization and mortality [7,15,16]. The K/DOQI guidelines for vascular access in haemodialysis recommended that 65% of all incident haemodialysis patients should start dialysis with AVF [17], which is associated with reducing access complications and improving patients' survival [16]. In the study population, only around 6.2-12.4% of patients have initiated haemodialysis with AVF. Furthermore, the trend of incidence of haemodialysis patients with AVF has not showed any improvement in recent decade.

NKF-K/DOQI guidelines states that, adverse outcomes of CKD such as loss of kidney function, kidney failure, and cardiovascular disease, can be prevented or delayed by detecting and treating CKD at earlier stages. This can be done

Table 3. Relation between pre-ESRD care periods and patient characteristics.

Outcome	Pre-ESRD care period				Total (%)	p-value
	>12m	6-12m	<6m	0m		
Age at referral time to nephrology care						
<14.9	5	0	1	2	8(2.8)	
15-29.9	11	3	16	24	54(18.6)	
30-44.9	14	5	21	43	83(28.6)	
45-59.9	15	5	28	46	94(32.4)	
≥60	4	7	17	23	51(17.6)	0.06
Sex						
female	20	8	27	57	112(38.6)	
male	29	12	56	81	178(61.4)	0.6
Referral source						
Emergency department	7	6	36	108	157(54.1)	
Other healthcare centres	11	5	11	17	44(15.2)	
Outpatient clinic	31	9	36	13	89(30.7)	<0.0001
Reason of referral to nephrologist						
Diseases of genitourinary system	4	4	2	1	11(4.4)	
Disease of circulatory system	12	4	31	39	86(34.1)	
Endocrine, nutritional and metabolic diseases & immunity disorders	19	11	41	69	140(55.6)	
Symptoms and signs indicate to renal diseases	2	0	4	9	15(6)	0.005
Diabetic nephropathy						
No	36	13	60	107	216(74.5)	
Yes	13	7	23	31	74(25.5)	0.6
Hypertensive nephropathy						
No	24	9	37	64	134(46.2)	
Yes	25	11	46	74	156(53.8)	0.97
Starting HD with AVF						
No	35	17	73	138	263(90.7)	
Yes	14	3	10	0	27(9.3)	<0.0001

HD= haemodialysis, AVF= arterio-venous fistula.

through routine laboratory measurements and eGFR. However, declining eGFR is associated with multiple complications such as hypertension, anaemia, malnutrition, neuropathy, and bone disease. All these complications can be treated at earlier stages of CKD [2]. In this study, many of the patients around 45.1-56.1% were referred to nephrology care because of endocrine, nutritional, and metabolic diseases; and 34.6-45.3% were referred because of uncontrolled blood pressure. The majority of those patients had not received nephrology care or the period of care was less than six months, while the dominant causes of ESRD were hypertensive nephropathy (50.8-60.7%) and diabetic nephropathy (20.4-29.1%).

This study shows that there is a significant association between the pre-ESRD care period and reasons of referral to nephrology care. The majority of patients with CKD had not

received pre-ESRD care or they received less than six months of care in all reasons of referral; most patients with ESRD were referred from emergency for urgent haemodialysis. A similar study that was conducted at Jeddah Kidney Centre in 2002, which used serum creatinine as an indicator of late referral, showed that the mean serum creatinine when first seen by a nephrologist was high, around 300 mmol/l [18]. Another screening study for CKD was conducted in Riyadh in Saudi Arabia using eGFR and laboratory measurements to detect CKD in the general population. This showed that around 7% of patients with CKD were not aware about their kidney status, 32% had known they had protein or blood in urine, and 11% had known they had kidney stones; for the last two, it was not mentioned whether they were followed up by nephrology care services [19]. These reflect delayed referral to nephrology

Table 4. Relation between initiating haemodialysis with AVF as outcome and different patient characteristics.

Predictor	Starting HD with AVF		Odds ratio	p-value
	No	Yes	(95% CIs)	
Age at referral time to nephrology care				
<14.9	6	2	1	-
15-29.9	48	6	0.4(0.06_2.3)	0.3
30-44.9	77	6	0.2(0.04_1.4)	0.1
45-59.9	84	10	0.4(0.06_2)	0.2
≥60	48	3	0.2(0.03_1.4)	0.1
Sex				
Female	135	12	1	-
Male	192	20	1.2(0.56_2.5)	0.6
Referral source				
Emergency department	181	7	1	-
Other healthcare centres	64	5	2(0.6_6.6)	0.2
Outpatient clinic	82	20	6.3(2.7_15.5)	<0.0001
Period of pre-ESRD care/month				
>12month	35	14	1	-
6-12month	17	3	0.4(0.1_1.7)	0.2
<6month	73	10	0.3(0.14_0.85)	0.02
0month	138	0	-	-
Reason of referral to nephrologist				
Diseases of genitourinary system	6	5	1	-
Disease of circulatory system	102	13	0.2(0.04_0.6)	0.005
Endocrine, nutritional and metabolic diseases & immunity disorders	152	9	0.07(0.02_0.3)	<0.0001
Symptoms and signs indicate to renal diseases	15	2	0.2(0.02_1.1)	0.06
Diabetic nephropathy				
No	243	27	1	-
Yes	84	5	0.54(0.2_1.4)	0.2
Hypertensive nephropathy				
No	150	11	1	-
Yes	177	21	1.62(0.77_3.5)	0.2

HD= haemodialysis, AVF= arterio-venous fistula.

care from other services such as primary care, diabetology, and cardiology. Also, where strong primary healthcare and health information systems are absent, it might reflect that there are many patients with CKD and its risk factors such as diabetes, hypertension, and cardiovascular disease undiagnosed in the general population or who were diagnosed but were not followed up consistently, which maybe why the majority of them were not referred to nephrology care in the early stages of their disease.

Due to time limitations for collecting data, a lack of national health information system in Saudi Arabia and some patients being referred from one healthcare centre to another, the laboratory measurements for renal function deterioration and eGFR were not usually available at referral time to nephrology

care in many medical records and even the reason of referral was often insufficiently explained. Furthermore, eGFR could not be calculated to determine at which CKD stage the patient had been referred to nephrology care due to missing or not reported information. The Modification of Diet in Renal Disease (MDRD) study equation to estimate GFR require taking into account serum creatinine concentration, age, sex, race, and body mass index [2]. Therefore, the preliminary indicators for pre-ESRD nephrology care were used in this study for detecting late referral to nephrology care. There is a potential selection bias in terms of the study population due to focusing on haemodialysis patients only. Patients with ESRD who initiate RRT with peritoneal dialysis or had pre-emptive renal transplanted; they would have been referred

to nephrology care at early stage.

Conclusion

This study provides information on the status of pre-ESRD care in Saudi Arabia and suggests that pre-ESRD care must be improved. This can be done through developing multidisciplinary strategies including; first, define patients at high risk and conduct regular screening to detect CKD in its early stages. Second, nephrology departments in healthcare centres should organise campaigns to educate healthcare practitioners including family physicians, diabetologists, cardiologists and internists about the necessity of referral patients with CKD to nephrology care at earlier stages of their illness. Third, improve communication channels between healthcare practitioners, and defining accurate criteria as to when to refer patients with CKD to nephrology care using a standardised tools [3]. Fourth, healthcare practitioners and social workers should organise programs to increase patients' awareness about their health status and potential complications. Fifth, patients at high risk of ESRD should be educated about their CKD and trained to better self-manage. As a part of a preventative strategy of chronic diseases, health information system must be developed in Saudi Arabia to evaluate population health and the quality of healthcare services consistently.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

AH designed study, created electronic database for data collection, collected data, performed statistical analyses, and drafted the manuscript. AM contributed in study design, coordination of the study, and reviewed the manuscript critically. HW contributed in statistical analyses, interpretation of data, and reviewed the manuscript critically. NB reviewed the manuscript critically.

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