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End-stage renal disease and renal replacement therapy in Kuwait—epidemiological profile over the past $4\frac{1}{2}$ years

K. El-Reshaid[1], K. V. Johny[1], T. N. Sugathan[2], A. Hakim[3], M. Georgous[3], M. R. N. Nampoory[3]

[1]Department of Medicine, [2]Department of Community Medicine, Faculty of Medicine, Kuwait University; [3]Dialysis Centres, Ministry of Public Health, Kuwait

Abstract. Data on end-stage renal disease (ESRD) patients in Kuwait were collected retrospectively and prospectively starting in mid-1988. The study period covered $4\frac{1}{2}$ years from 1 January 1986 to 30 June 1990. Epidemiological characteristics of ESRD patients and their disposal by dialysis and transplantation were analysed and compared with previous reports from Kuwait, neighbouring countries, Europe, and USA. A total of 647 patients received renal replacement therapy (RRT) in Kuwait during the study period. This gave an incidence rate of 72 patients per year per million of population. The prevalence rate for patients on maintenance dialysis was 80.6 per million population in mid-1988. Nearly one-fifth of total patients (19.6%) were older than 60 years of age and one-third (30.8%) were identified as 'high risk' category. As for Kuwaiti nationals alone on RRT 29.7% were above 60 years of age and 44.2% were high-risk patients. We have noticed a steady decline in the number of patients who accepted continuous ambulatory peritonial dialysis (CAPD) for dialytic support.

Chronic tubulointerstitial disease resulting from atrophic pyelonephritis was the leading cause of ESRD amongst both Kuwaiti nationals and expatriates. Though diabetic nephropathy was only the third leading cause of ESRD (14.7%) in the total population, it was more frequent (21.2%) among Kuwaitis. The gross mortality rate on dialysis was 14.7%. The major causes of death were related to cardiovascular diseases (60%) and sepsis (24.2%). Our analysis showed that age of the patient at admission to dialysis contributed to overall mortality, but it was not an isolated risk factor whereas diabetic nephropathy (relative risk 1.9) and associated serious co-morbid illness/es (relative risk 30.3) were. Despite strict precautionary measures in the dialysis units and early use of erythropoietin, 68 new patients were detected to be HBsAg positive, 85% of whom remained persistently antigenaemic for more than 6 months. At follow-up 9.8% (4/41) had died of liver failure.

The 50 months patient survival for patients who received unrelated kidney transplantation (abroad) was lower than in those who received live related kidneys in Kuwait. The most distressing observation was, however, the very high patient loss associated with imported cadaver kidneys transplanted in Kuwait compared to those who received cadaver kidneys harvested locally (65% versus 94.8% respectively at 16 months).

Key words: end stage renal disease; Kuwait; dialysis; transplantation

Correspondence and offprint requests to: Dr K. El-Reshaid, Department of Medicine, Faculty of Medicine, P.O. Box 24923, Safat, 13110 Kuwait

Introduction

Kuwait is located on the north-eastern part of the Arabian peninsula and has an area of 17818 km^2 (6960 sq. mile). In mid-1988 it had a population of 1.96 million of which 0.78 million (39.8%) were Kuwaiti nationals. Renal replacement therapy (RRT) was initiated in Kuwait at a single dialysis unit in 1976 with a few patients on haemodialysis (HD). Intermittent cycling peritoneal dialysis (IPD) was provided first in 1979 and continuous ambulatory peritoneal dialysis (CAPD) in 1982. In the later years the dialysis facilities were expanded to three centres with over one hundred dialysis stations. The first renal transplantation was done in Kuwait in 1979 and a specialized centre for organ transplantation was commissioned in 1988.

Maintenance dialysis is provided entirely free of cost for nationals and expatriates by the Ministry of Public Health. Acceptance to the maintenance dialysis programme is relatively liberal and restricted only when end-stage renal disease (ESRD) co-existed with other major life-threatening medical illnesses such as malignancies, advanced cardiac decompensation, irreversible brain damage, hepatic failure, etc.

The aim of the study was to examine the epidemiological pattern of ESRD in Kuwait and the relevance of various forms of RRT to its disposal.

Subjects and methods

Data on ESRD in Kuwait were collected retrospectively and prospectively starting in mid-1988 from the three dialysis centres and the organ transplant centre. The study period covered 4½ years from 1 January 1986 to 30 June 1990. A total of 647 patients received RRT in Kuwait during the study period. Those patients who received dialytic support for less than 6 weeks and recovered to remain free off dialytic support were excluded from analysis.

Haemodialysis and peritoneal dialysis were the two widely accepted modes of dialytic support. Patients with unstable cardiovascular status, vascular access problems or with contraindication to the use of heparin were primarily chosen for IPD. CAPD was provided for self-motivated patients only. Except for two patients who used cycling peritoneal dialysis at home and those on CAPD, all others received institutional dialysis. Patients with positive hepatitis B surface antigen were dialysed in separate rooms.

Most patients received 12 h of HD per week in three sessions. Acetate bath was mostly used and nearly one-tenth of patients were on bicarbonate dialysis. Hollow-fibre dialysers made of cuprophane membrane were largely used. There was no re-use of dialysers. Patients on IPD received 2-litre hourly exchanges for 24 h, usually twice weekly using an automated cycler machine. Y-disconnect system was used in CAPD.

Patients who were medically fit received renal transplants either locally in Kuwait or at centres abroad depending on the availability of kidneys. Sources of kidneys included live related, live unrelated, and cadaver donors. The local renal transplant programme was dependent mainly on live related and emotionally motivated kidney donors. Live unrelated kidney transplantation was largely carried out abroad. Cadaver kidneys were either locally harvested or imported from western countries. Post transplant immunosuppressive treatment was a triple-drug regime using cyclosporin, azathioprine and prednisolone except for some well-matched live-related pairs.

Patients with unstable cardiovascular status or other advanced non-renal diseases were categorized as high-risk group and were largely supported by dialysis.

Statistical methods

The data were analysed using the BMDP statistical package. Cumulative probability of survival of patients on dialysis and after renal transplantation was determined by using product limit survival analysis. The differences in survival time among various groups were tested by using generalized Wilcoxon test. The relative risk for various factors likely to contribute to mortality was studied by using Cox proportional hazard regression model.

Results

During the study period of 54 months 647 new patients received renal replacement therapy (RRT) in Kuwait. This gave an incidence rate of 72 patients per million of population per year. The prevalence rate for patients on maintenance dialysis was 80.6 per million population during 1988. The epidemiological characteristics of the patients are shown in Table 1. There were more expatriates with ESRD (58.4%) than Kuwaiti nationals; however, the incidence of ESRD was 78 per million population among Kuwaiti nationals and 70.4 for expatriates. In general, males were 1.8 times the females, but amongst the expatriates alone the males were 2.26 times the females. Nearly one-fifth of total patients (19.6%) were over 60 years of age and one-third (30.8%) were in the high-risk category. As for Kuwaiti nationals alone on RRT, 29.7% were over 60 years of age and 44.2% were high-risk patients.

Aetiology of ESRD

The underlying renal diseases that progressed to ESRD in patients are listed in Table 2. In the majority, diagnosis was inferred from the clinical data whereas it was histologically confirmed in patients in whom a renal biopsy was indicated. Chronic tubulointerstitial disease resulting from atrophic pyelonephritis was the leading cause amongst both Kuwaitis and expatriates. Though diabetic nephropathy was only the third leading cause of ESRD (14.7%) in the total population, it was more frequent amongst Kuwaitis (21.2%) and had reached the same frequency as that of primary glomerulonephritis. All those patients except for two had non-insulin-dependent diabetes mellitus. Adult polycystic kidney disease and lupus nephritis leading to ESRD were each seen in 3.7% of Kuwaiti nationals on dialysis. It was also noted that hypertensive nephrosclerosis (0.7%) and obstructive uropathy (2.2%) were relatively rarer causes of ESRD in Kuwaiti nationals.

Disposal of patients with ESRD

The disposal of patients with ESRD is shown in Table 3. Sixteen percent (103 patients), all expatriates, returned to their country of origin and were lost to follow up. Renal transplantation was the major mode

Table 1. Epidemiological characteristics of patients on RRT

	Kuwaiti Nationals	Expatriates	Total	Percent
1. Sex				
Males	150	262	412	(63.7)
Females	119	116	235	(36.3)
Total (%)	269 (41.6)	378 (58.4)	647	(100)
2. Median age*	50	40.5	45	
3. Over 60 years of age* (%)	80 (29.7)	47 (12.4)	127	(19.6)
4. High-risk group* (%)	119(44.2)	80 (21.2)	199	(30.8)
5. Cumulative survival (%) at 50th month*	45	62	52.5	

*Differences between Kuwaiti nationals and expatriates were significant at $P<0.05$.

Table 2. Aetiology of renal disease in the study group

Renal disease	Kuwaiti *n* (%)	Non-Kuwaiti *n* (%)	Total *n* (%)
Tubulointerstitial disease	105 (39.0)	145 (38.4)	250 (38.6)
Primary glomerulonephritis	57 (21.2)	98 (25.9)	155 (24.0)
Diabetes mellitus (type 1 & 2)	57 (21.2)	38 (10.1)	95 (14.7)
Obstructive uropathy	6 (2.2)	27 (7.1)	33 (5.1)
Adult polycystic kidney disease	10 (3.7)	9 (2.4)	19 (2.9)
Lupus nephritis	10 (3.7)	8 (2.1)	18 (2.8)
Hypertension	2 (0.7)	12 (3.2)	14 (2.2)
Others	12 (4.5)*	17 (4.5)**	29 (4.5)
Aetiology uncertain	10 (3.7)	24 (6.3)	34 (5.3)
Total	269 (100)	378 (100)	647 (100)

Others: *amyloid 3; Fabry's disease 2; analgesic abuse 2; polyarteritis nodosa (PAN) 2; atheroembolic 1; multiple myeloma 1; renovascular 1. **amyloid 8; medullary cystic disease 3; PAN 3, multiple myeloma 1; Alport's 1; Goodpasture's 1.

Table 3. Disposal of patients with end-stage renal disease

Disposal		Total	%
Left for country of origin		103	16
Transplantation			
A. Live donors		227	35
Related	130		
Emotionally related	12		
Unrelated	83*		
B. Cadaver donors		62	9.6
Locally harvested	19		
Imported	40		
Abroad	3		
Overall deaths on dialysis		95	14.7
Remaining on dialysis		162	25
Total	287	647	100

*80 of these were transplanted abroad.

of disposal (287 patients) and constituted 52.8% of those remaining on treatment in Kuwait. Twenty-four patients (8.3%) received renal transplantation without dialytic support prior to surgery. Two hundred and four patients (71% of those transplanted) underwent renal transplantation locally and the rest (83 patients) while abroad. The local transplant programme depended largely on live related donors (130 patients). There were 12 emotionally related and four genuinely motivated voluntary donors. Fifty-nine patients were transplanted in Kuwait with cadaver kidneys either locally harvested (19 patients) or imported from abroad (40 patients). Eighty-three patients received kidneys while abroad, 80 from voluntary donors and three from cadavers. During the study period 10 patients were regrafted. The median duration on dialysis prior to kidney transplantation was 4 months. There was no difference in the median duration on dialysis prior to kidney transplantation between Kuwaiti nationals, expatriates, those transplanted locally or abroad (4, 5, 4, and 6 months respectively). Generally an extra of 10–15 patients per year continued to remain on maintenance dialysis leading to a cumulative increase in the dialysis population.

Dialytic therapy

Excluding the 24 patients who underwent renal transplantation without preoperative dialytic support, 486 patients received HD (78%), 105 IPD (16.9%) and 32 CAPD (5.1%). Five patients who were initially on HD were changed to IPD because of cardiovascular instability. Similarly five patients on IPD (10.9% of total IPD patients) were transferred to HD because of catheter failure.

During the study period 95 patients on dialysis expired, an overall gross mortality rate of 14.7%. The major causes of death were related to cardiovascular diseases (60%) and sepsis (24.2%) (Table 4). The cumulative survival for all patients on maintenance dialysis was 52.5% at 50 months whereas it was only 22.5% for the elderly (above 60 years of age) and 20% for those with diabetic nephropathy (Figure 1). There was also a significant difference ($P < 0.05$) in the cumulative survival for Kuwaiti nationals (45%) and expatriates (62%) at 50 months (Table 1). The overall mortality for patients who remained on dialysis was 35.7% while that for patients who were transferred from HD to IPD or *vice-versa* was 60% and 61.5% respectively. Further, analysis of the relative risk factors likely to contribute to mortality, viz. nationality, age, sex, original renal disease, associated serious non-renal diseases (high-risk category) and mode of dialytic treatment received, showed that presence of serious associated non-renal diseases (relative risk 30.3) and diabetic nephropathy as the underlying renal disease (relative risk 1.9) were the two significant contributory factors.

HBV infection in dialysis units

Despite strict isolation of positive patients and use of erythropoietin to limit blood transfusion requirements, 45% of 228 patients at the end of the study period were either HBs antigen (6.1%) or HBs antibody (39%) positive. As for the 75 unvaccinated staff members working in the units, 55% were HBs antibody positive and another 1.3% antigen positive. Sixty-eight new patients were HBs antigen positive, 85% of whom

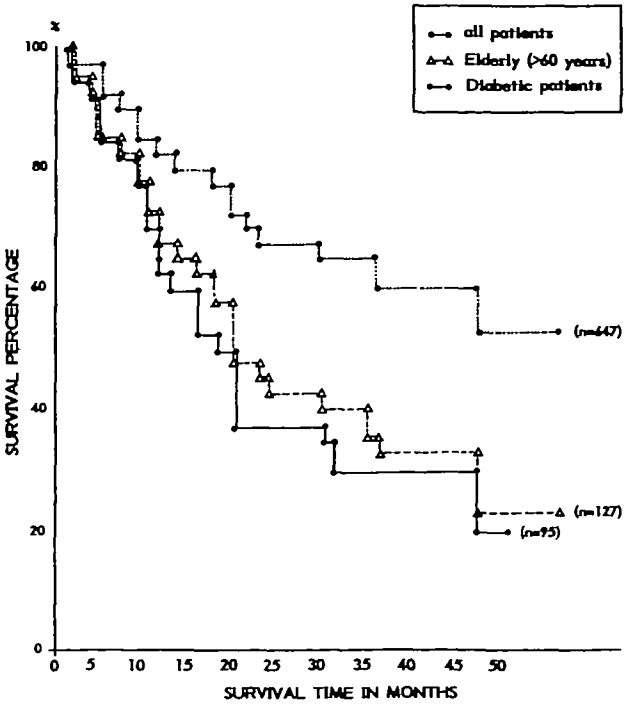

Fig. 1. Acturial survival of patients on dialysis.

Table 4. Proportional mortality (PM) by cause

Causes of death	No.	PM (%)
Cardiovascular	57	60.0
Sepsis	23	24.2
Hepatic failure	2	2.1
Cerebrovascular	2	2.1
Refusal to be dialysed	5	5.3
Inadequate dialysis	3	3.2
Total	95	100

remained persistently antigenaemic for more than 6 months. At follow-up 9.8% (4/41) had died of liver failure.

Outcome on renal transplantation

The patient and graft survival following renal transplantation are shown in Table 5. The patient and graft survival at 50 months for the 130 live-related renal transplants, all done in Kuwait, were 87.5% and 82.5% respectively; the 80 live unrelated transplants, all done abroad, were 77.5% each. As for patient survival, the above difference between the two groups was significant ($P=0.029$) (Figure 2).

The outcome of cadaver renal transplantation differed significantly depending on whether the kidneys were imported or locally harvested (Figure 3). At 16 months the survival for patients receiving imported cadaver kidneys was only 65% compared to 94.8% for patients who received locally harvested kidneys ($P=0.04$). At 50 months the patient survival dropped to 52.5% for imported cadaver kidney recipients (Table 5). Thirty-five percent of patients (14/40) who

Table 5. Cumulative survival for patients and graft

Source of kidney +	*n*	Cumulative survival (%)			
		At 16 month		At 50 month	
		Patient	Graft	Patient	Graft
Live donors					
Related	130	92*	92.5	87.5*	82.5
Unrelated	80	80*	90	77.5*	77.5
Cadaver donors					
Locally harvested	19	94.8*	79	—	—
Imported	40	65*	72	52.5	72.0

+ Live related and cadaver transplants are undertaken in Kuwait whereas live unrelated transplants are performed abroad.
* $P<0.05$.

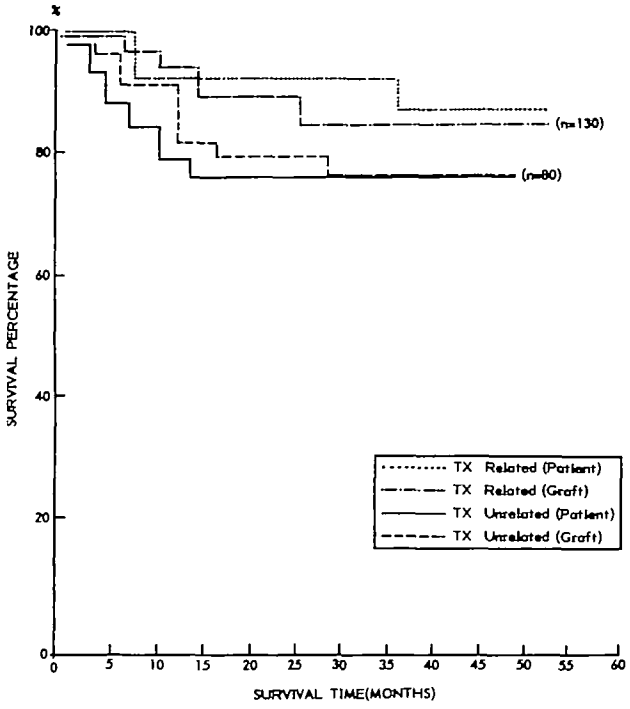

Fig. 2. Acturial patient and graft survival for unrelated and related kidney transplantation.

received an imported cadaver kidney died during the study period; 10 deaths occurred in the first month following transplantation. In contrast, only one patient (5%) died from the 19 who received locally harvested kidneys.

Discussion

Information on the epidemiological characteristics of ESRD and RRT from the Arab countries is limited. Available data on the aetiology of ESRD and quality of RRT are affected by the short duration of observation and limited geographical area covered by some studies [1,2]. Some others are handicapped from inadequate facilities available for the care of patients with chronic renal failure [3,4]. Our study has, however,

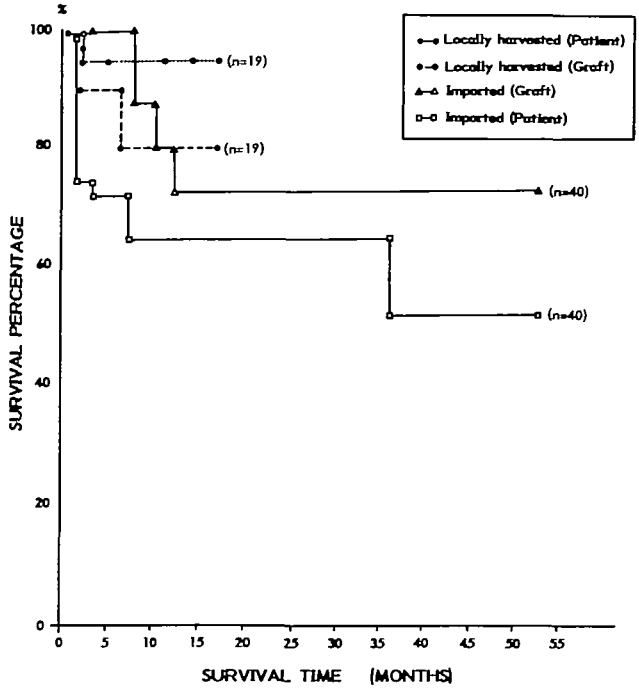

Fig. 3. Acturial patient and graft survival for cadaver renal transplantation.

covered the whole country. We believe it reflects the true pattern of the epidemiological characteristics of ESRD and RRT in Kuwait, because by 1988, with the establishment of three dialysis units having more than 100 dialysis treatment stations, an organ transplant centre and improved patient referral and speciality services, the programme had reached some maturity and stability. Further, the relatively liberal policy of accepting ESRD patients to the dialysis programme that is fully financed by the government has helped to obtain near factual data on ESRD in this Arab population.

Our observation of an incidence rate of 72 new patients with ESRD per million population (including Kuwaitis and expatriates) is thus higher than that reported from Kuwait earlier [3] but should be more realistic. The incidence rate of ESRD for Kuwaiti nationals alone was 77 per million population and for expatriates it was 71.2. An incidence rate of over 70 new patients with ESRD per million population is much higher than that reported by EDTA in many European countries (42.3 p.p.m.) [5] but lower than that of the USA (190 p.p.m.) [6]. The prevalence rate of patients on maintenance dialysis observed in this study is lower than that reported earlier from Kuwait (100 p.p.m.) [3]. This most probably reflects an increased disposal of patients through transplantation during the later years. Up to 1983 fewer than 30 patients received transplantation in 1 year whereas the number rose between 41 and 84 patients per year during our study period. The incidence of ESRD in Kuwaiti nationals does not differ between males and females (Table 1). However, in the expatriate population there are more males with ESRD (69.3%) which reflects only the male preponderance in the expatriate population in Kuwait (61.7%) [7]. In Kuwait only 3.5% of the Kuwaiti nationals and 2.1% of the total population are over 60 years of age [7]. However, 29.7% of Kuwaitis and 19.6% of total patients on RRT are in this older age group, which suggests a higher incidence of ESRD in the elderly.

The causes of underlying renal disease leading to ESRD in our study have differed from the earlier report from Kuwait [3] and that from European countries [5,8]. An accurate aetiological diagnosis of ESRD can be difficult when patients present to the hospital in the late stages of their disease. Kuwait being a small country with early referral facilities to a specialist centre, relevant clinical and laboratory parameters are available for most patients included in this study that a careful analysis of information has helped in arriving at an aetiological diagnosis in nearly 95% of the patients.

The earlier report from Kuwait [3] had observed glomerulonephritis as the most frequent underlying disease leading to ESRD in contrast to our finding of chronic tubulointerstitial disease. While this difference may be a reflection of the inherent difficulties faced by clinicians in arriving at an exact aetiological diagnosis of ESRD, the same argument cannot hold true of diabetic nephropathy as a cause of ESRD in Kuwait. In 1983 only 2.2% of their patients on dialysis had diabetic nephropathy, whereas with our observation made a few years later the incidence was 14.7% for all patients and 21.2% in Kuwaiti nationals. This observation indicates a true change in the epidemiological pattern and may be the outcome of prolonged survival of type II diabetics in Kuwait with the improved general medical care facilities and a more liberal admission policy to maintenance dialysis.

Recent reports from Saudi Arabia have shown that diabetic nephropathy is the cause of ESRD in 13.7% of patients on RRT [1,2]. A similar trend of increased diabetic ESRD in the dialysis units has been reported from developed countries such as USA (35%) [6] and Europe (13.1% and 10.6%) [5,8] in the recent years. This finding of diabetic ESRD as a major aetiological factor in Kuwaiti nationals on dialysis is a distressing observation. They generally form a high-risk group on dialysis, having an overall mortality rate of 53% and a 50-month survival rate of only 20%. They also have only a poor chance for optimal rehabilitation [16]. The prevalence of type I diabetes in Kuwait is 2% and that of type II is 8% [9]. However, only 2/57 Kuwaiti nationals and 0/42 expatriates on dialysis for diabetic ESRD had type I diabetes. This indicates that ESRD from type I diabetes is infrequent in our dialysis units and this deserves further studies. A lower incidence of obstructive uropathy in our ESRD population compared to that reported from Saudi Arabia (5%) [1,2] and Sudan (12%) [4] is noted. Renal stone disease, though frequent in Kuwait [10] seldom causes ESRD in our experience. Hypertensive ESRD is also infrequent in our dialysis units (2.2%) as compared to the European experience (9.6%) [8]. These observations

may reflect the preventable nature of some of the underlying renal diseases that lead to ESRD.

The first-year mortality rate of 50% on dialysis in 1965 had improved to 15% in 1980 due to technological advances in dialysers and machines and also from improved knowledge leading to more standardization of dialysis treatments [11]. However, the overall mortality rate on dialysis in our hands has not changed since the earlier report from Kuwait [3] and the cumulative first-year mortality has remained at 17%. This lack of further improvement in mortality with time in a country where inadequate dialysis is not a problem and reuse of dialysers is not practised, is clearly related to the present liberal policy of admitting high-risk patients to the maintenance dialysis programme [6,16–22]. The observed lower survival rate in Kuwaiti nationals compared to that in the expatriate population in Kuwait further supports this conclusion (Table 1). The overall mortality rate in our hands is still higher than that reported from Europe (9.7%) [13] and Japan (8.8%) [14] but lower than that in USA (23%) [15].

Large studies conducted to assess the risk factors in dialysis patients using survival analysis [17–20] or Cox regression model [21,22] have suggested that advanced age, male sex, diabetic nephropathy, and presence of other serious co-morbid conditions contributed significantly to mortality. Our analysis has shown that the age of the patient at admission to maintenance dialysis treatment contributes to the overall mortality but is not an isolated risk factor, whereas diabetic nephropathy and other associated illnesses are. The major cause of death in our hands is related to cardiovascular problems (60%) while inadequate dialysis contributed only 3% to the overall mortality. Infections, which are inherent complications associated with the technique of dialysis itself, related to haemoaccess or peritoneal catheters, contributed to 60.5% of the non-cardiac causes of death (Table 4).

CAPD is assuming an increasingly important role in the therapy of ESRD in Europe [8] and USA [6]. A recent large multicentre study from England showed that CAPD was utilized twice as often as HD for managing new patients. In Kuwait there is a steady decline in the number of patients who accept CAPD for maintenance dialysis, despite enthusiastic encouragement given by the dialysis staff for this modality of dialytic support. Young patients generally prefer renal transplantation even when the donor is unrelated and the practice is uncontrolled. Fear of possible infections consequent upon the treatment itself [23], lack of self motivation in patients, liberal governmental support for HD and IPD facilities in the hospitals, and family preferences for institutional IPD for the elderly and dependent patients have contributed to this observed decline in CAPD patients in Kuwait.

Previous studies have shown that hepatitis B is endemic in neighbouring countries [24] and their dialysis units [1,2]. Our study confirms the high prevalence of hepatitis B infection among our dialysis patients and the lack of immunogenic protection manifested by a more prolonged antigenaemia and serious liver disease (9.8% fatality) [25].

A significant proportion of ESRD patients in Kuwait travel abroad for live unrelated renal transplants from voluntary donors. The 50-months patient survival in this group was lower than in those who received live related kidneys. Recipients with high-risk non-renal diseases undergoing renal transplantation from poorly HLA matched donors [26] under suboptimal medical conditions best explain this relatively poor outcome. The most distressing observation is, however, the very high patient loss associated with imported cadaver kidneys transplanted in Kuwait, compared to those who received cadaver kidneys harvested locally (65% versus 94.8% respectively at 16 months). This is clearly explained by the poor quality of such imported kidneys, with prolonged cold ischaemia time (>48 h) [27] and a high incidence of septic complications [28], resulting in patient loss in the immediate post-transplant period.

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