ORIGINAL ARTICLE

PREDICTORS OF SURVIVAL AMONG END STAGE RENAL FAILURE PATIENTS UNDERGOING DIALYSIS TREATMENT IN PAHANG FROM 2000 TO 2004

AJ Hamid[1] and MT Azmi[2]

[2]Department of Community Health, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latiff, 56000 Cheras, Kuala Lumpur, [1]Bahagian Kesihatan Awam, Jabatan Kesihatan Negeri Sabah.

ABSTRACT

Introduction : A retrospective cohort study was conducted among ESRD who received dialysis treatment (Haemodialysis and CAPD) in all government hospitals in the State of Pahang from 1st January 2000 to 31st December 2004.

Objective : The aim of the study was to identify factors affecting the survival of patients undergoing dialysis in the state of Pahang.

Methods : Survival time was measured from the date of dialysis until the subjects died, lost to follow up or until the end of the study period at 31st December 2004.

Results : Diabetes mellitus was the major cause for ESRD (33%) out of 132 subjects eligible for the study. Seven (7.1%) and five (15.2%) deaths occurred among haemodialysis and CAPD patients respectively, but statistically of no difference between the two treatments (log-rank, p=0.093). Factors influencing the survival of haemodialysis patients were diabetes mellitus (p=0.014), albumin (p=0.0005), creatinine (p=0.020) and hemoglobin level (p=0.002), while age of treatment and diabetes mellitus affecting the survival of CAPD patient. Cox Proportional Hazard Regression showed that haemodialysis subjects with low albumin (HR 0.669 df 95% 0.513 - 0.873) and hemoglobin (HR 0.403 df 95% 0.225 - 0.720) level had lower survival rate but none for CAPD.

Conclusion : Good nutritional status, higher hemoglobin level and prevention of diabetes mellitus are important for the survival of haemodialysis patient.

Key Words : Survival, End Stage Renal Failure, Dialysis

Received Jan, 2009; Accepted Jun 2009

Correspondence to: Dr Abdul Hamid Jaafar,
Bahagian Kesihatan Awam,
Jabatan Kesihatan Negeri Sabah
Tingkat 1, Rumah Persekutuan,
Peti Surat No. 11290,
88814 Kota Kinabalu.
Tel: 019-9302212/ 088-265960 Fax: 088-217740
(e-mail: dramied@yahoo.com.sg / drabdhamid@moh.gov.my)

INTRODUCTION

Kidney is an important organ in humans. Any disease that can affect its function can cause various problems to our body such as accumulation of body waste, acid-base imbalance and reduction of hormone production. End stage renal disease failure (ESRD) is a spectrum of chronic renal failure where there is irreversible function loss which leads to a clinical syndrome known as uraemia.

The incidence and prevalence of ESRD is increasing every year worldwide and almost all of them are related to the increasing incidence of diabetes mellitus[1]. In United State of America (USA) the number of patients is expected to increase to 600,000 in 2008 from 256,000 in 1998[2]. The same scenario also happened in Malaysia where the prevalence increased from 59 in 1980 to 8954 in 2002[3]. There are two kinds of treatment commonly delivered to these patients especially when the conservative treatment fails to slow down the progression of the disease: The Renal Replacement Therapy (RRT) which includes haemodialysis and continuous ambulatory peritoneal dialysis (CAPD), and Renal Transplantation[4,5]. In Malaysia, haemodialysis treatment is the most commonly received by ESRD patient (80 to 90%) as compared to CAPD[3].

The dialysis treatment has benefitted most of the ESRD patients by reducing their morbidity and mortality. In Malaysia the number of patients receiving dialysis treatment has increased from 59 in 1980 to 10,000 in 2003 but the mortality rate has been stable at 10% per year since 1980 till 2003 although there is an advancement of dialysis technology and increase of dialysis facilities in the country[3].

A lot of studies has been done to identify the factors that can influence the patients' mortality. One study found that CAPD patients have 19%2. higher mortality rate (RR 1.19; $p< 0.001$) compared to haemodialysis, but another revealed that CAPD patients have a 27% lower mortality (RR 0.73; 95% CI: 0.68-0.78)[6,7]. Yet another study has found a better survival rate among CAPD patients for the first 2 years of treatment (RR 0.65; 0.59-0.72, $p<0.001$)[8]. The increasing age, alcoholism and the present diabetes mellitus and cardiovascular disease (CVD) have reduced the survival rate, but it is not affected by hypertension or sex. It was shown that the survival was reduced by increasing of age, smoking and the presence of diabetes mellitus, ischemic heart disease, arteriosclerosis and cancer[9].

Studies found that malnutrition factors such as low albumin, urea and creatinine level reduces the patient's survival rate[10,11]. Surprisingly higher cholesterol level will benefit the patients survival especially for those with systemic inflammation[12,10,11]. Meanwhile body mass index of more than 30kg/m^2 increased the survival rate of haemodialysis patients[13,14,15,16]. Other factor identified influences the survival rate was the adequacy of treatment, measured by Kt/V (K= dialysis clearance, t = duration of treatment session, V = volume of body fluid), whereby the higher Kt/V can reduce the mortality risk[17]. The Kt/V value of 1.2 is considered adequate for the dialysis of patients [18,19].

It is clear that different studies will give different findings regarding factors affecting the survival of patients especially in the early phase of treatment. It could be happens because of the different methodology or the cohort of patients being used and also biases that can exist in the study.

GENERAL OBJECTIVE

To measure the survivorship of ESRD patient who received dialysis treatment at the government hospital in the state of Pahang and the influencing factors.

SPECIFIC OBJECTIVES

To identify sociodemographic characteristics (age, sex, ethnicity, educational level, marital status, income and method of payment) of which affected the survival of the patients and also according to the method of dialysis.

To compare the survivorship between patients who received haemodialysis and CAPD for the 5 years period of treatment (5-year survival), and also according to the sociodemographic factors (age of first treatment, sex, ethnicity, educational level, marital status, income and method of payment); co-morbidities like diabetes mellitus, hypertension and cardiovascular disease; nutritional parameters like body mass index (BMI), albumin, cholesterol, triglyceride, urea and haemoglobin level; and the adequacy of dialysis by Kt/V value

METHODOLOGY

This was a survival analysis study of retrospective cohort design, using clinic-held records of ESRD patients, who were receiving dialysis treatment (Haemodialysis and CAPD) in all government hospitals in the State of Pahang from 1st January 2000 to 31st December 2004. The subjects were selected through universal sampling technique and the required sample size was counted by using "Power and Sample Size Calculation' version 2.1.31 software. A total of 114 subjects were needed in this study. The required data were extracted from the record of dialysis clinic and were entered into the statistical software. Survival time was measured from the date of initial dialysis until the subjects died, lost of follow-up or achieving the end of the study period at 31st December 2004.

Inception cohort

The patients recruited to the study were drawn from all patients referred to in the government dialysis centres in Pahang between 1 Jan 2000 and 31 Dec 2004. They were further followed up until 30 June 2005 to ascertain their survival outcome. Patients were included in this analysis if their disease onset occurred before 1 January 2000 and the first dialysis treatment was in or after 1 January 2000. The disease onset defined as those having the symptoms of and diagnosed as ESRD by the nephrologist. Patients who were first referred and received dialysis treatment before 1 January 2000, although had had a disease onset prior to this date, were excluded. All the patients included satisfied the criteria for ESRD. Detailed clinical, laboratory and other relevant information was abstracted from the patients' records, much of which is held on their respective records. The patients were subdivided into those undergoing haemodialysis and peritoneal dialysis.

Censored cases

The patients who were still alive at the end of the study period (31st December 2004) or to have unknown outcome were classified as censored cases.

Statistical Analysis

Statistical analysis was conducted using SPSS version 11.5. The basic characteristics of the subjects were tested χ^2-test for qualitative data and t-test for normally distributed quantitative data, whereas for non-normally distributed quantitative data were analysed by Mann-Whitney U test. Survival distribution of the patient was calculated by Kaplan-Meier and the difference of survival rates between the independent factors were tested by log-rank test. Multivariate survival analysis was then carried out using Cox Proportional Hazard Regression. Level of significance was determined by using the 95% confidence interval and p-value <0.05 (two-tailed).

RESULT

A total of 132 (67%) subjects were eligible out of 197 registered and receiving dialysis treatments from 1st January until 31st December 2004. The age factor was normally distributed with the min and median at 50 and 51 years respectively. There were more male subjects (59.8%), of Malay ethnicity (65.7%), married (82.6%), have secondary or higher educational level (59.1%), income of less than RM1000 per month (61.4%) and have free or fully subsidised treatment from the government (TABLE 1). diabetes mellitus has been identified as major cause of ESRD (33%) but for the majority of the cases, the cause were unknown (40.2%) (TABLE 2).

Table 1 Sociodemographic Distribution Of The Subjects

Factors	Characteristics	No of subject (n=132)	%
Sex	Male	79	59.8
	Female	53	40.2
Age of treatment	< 25 year old	7	5.3
	25 – 34	14	10.6
	35 – 44	16	12.1
	45 – 54	47	35.6
	55 – 64	30	22.7
	65 – 74	15	11.4
	> 74 year old	3	2.3
Ethnic	Malay	87	65.9
	Non- Malay	45	34.1
Marital status	Married	109	82.6
	Single	23	17.4
Educational level	Primary school and less	54	40.9
	Secondary school and upper	78	59.1
Income	< RM1000	81	61.4
	> RM1000	51	38.6
Method of payment	Self	48	36.4
	Free/ fully subsidised	84	63.6

Table 2 Cause Of ESRD

Cause of ESRD	No of subjects (%)
Unknown	53 (40.2)
Diabetic nephropathy	43 (32.6)
Chronic Glomerulonephritis	21 (15.9)
Obstructive Uropathy	7 (5.3)
Analgesic nephropathy	5 (3.8)
Polycystic kidney	3 (2.3)

Further analysis showed no sociodemographic factors difference between haemodialysis and CAPD patients except for the method of payment whereby more patients were receiving free treatment for both hemodialyses (55.56%) and CAPD (87.88%) (TABLE 3). However there were differences between the 2 groups for Diabetis Mellitus, hypertension, albumin, cholesterol and urea level and also Kt/v value. Haemodialysis patients are more likely to be hypertensive but not diabetic or had cardiovascular disease compared to CAPD .

Haemodialysis patients also have a higher albumin and urea level but not for cholesterol and Kt/V value as compared to CAPD patients.

During the 5 years period of observation (TABLE 4) 7.1% of haemodialysis and 15.2% of CAPD patients died, and the mortality incidence rate for CAPD subjects were higher (100.10 per 100 persons years) as compared to haemodialysis subjects (3.26 per 100 persons years), but the difference of mortality incidence between the two treatments were not significant (RR 2.35, 95% CI: 0.69-7.97).

Table 3 The Comparison Between Haemodialysis and CAPD Subjects According To Sociodemographic Factors, Smoking, Nutritional Parameter and Kt/V

Factors	Characteristic	HD *n* (%)	CAPD *n* (%)	*p*	*RR* (95% CI)
Sex	Male	58 (73.4)	21 (26.6)	0.608	0.81 (0.36-1.83)
	Female	41 (77.4)	12 (22.6)		1.0
Age of treatment	**Mean**	50.67	48.33	0.332[a]	
Ethnic	Malay	61 (70.1)	26 (29.9)	0.072	1.0
	Non- Malay	38 (84.4)	7 (15.6)		2.31 (0.92-5.851)
Marital status	Married	81 (74.3)	27.3 (25.7)	0.691	1.0
	Single	18 (78.3)	5 (21.7)		1.24 (0.42-3.66)
Educational level	Primary school and less	45 (83.3)	9 (16.7)	0.066	2.22 (0.94-5.26)
	Secondary school and upper	54 (69.2)	24 (30.8)		1.0
Income	< RM1000	65 (80.2)	16 (19.8)	0.079	2.03 (0.91-4.51)
	> RM1000	34 (66.7)	17 (33.3)		1.0
Method of payment	Self	44 (91.7)	4 (8.3)	**0.001**	5.80 (1.90-17.74)
	Free/ fully subsidised	55 (65.5)	29 (34.5)		1.0
Smoking	Non-smoker	65 (78.3)	18 (21.7)	0.253	1.59 (0.72-3.55)
	Smoker	34 (69.4)	15 (30.6)		1.0
diabetes mellitus	Present	30 (61.2)	19 (38.8)	**0.005**	0.32 (0.14-0.72)
	Absent	69 (83.1)	14 (16.9)		1.0
Hypertension	Present	78 (71.6)	31 (28.4)	**0.047**	0.24 (0.05-1.08)
	Absent	21 (91.3)	2 (8.7)		1.0
Cardiovascular disease (CVD)	Present	13 (54.2)	11 (45.8)	**0.009**	0.30 (0.12-0.77)
	Absent	86 (79.6)	22 (20.4)		1.0
Body mass index (BMI)	**Mean**	22.93	24.62	0.069[a]	
Albumin (g/l)	**Mean**	40.81	36.60	**0.0005**[a]	
Cholesterol (mmol/l)	**Mean**	4.82	5.55	**0.001**[a]	
Triglyceride (mmol/l)	**Mean**	2.13	2.43	0.370[a]	
Kreatinin (umol/l)	**Mean**	885.87	866.99	0.601[a]	
Urea (mmol/l)	**Mean**	19.92	16.05	**0.0005**[a]	
Haemoglobin (g/dl)	**Mean**	10.13	10.23	0.525[a]	
Kt/V	**Mean**	1.51	1.98	**0.0005**[a]	

[a]Mann-Whitney U test

Table 4 The Comparison Of Mortality According To The Type Of Dialysis

Status	Alive n (%)	Died n (%)	Incidence per 100 persons years	p	RR (95% CI)
Haemodialysis	92 (92.9)	7 (7.1)	3.26	0.174[a]	2.35 (0.69 - 7.97)
CAPD	28 (84.8)	5 (15.2)	100.10		1.0

[a] χ^2–test with Yates correction

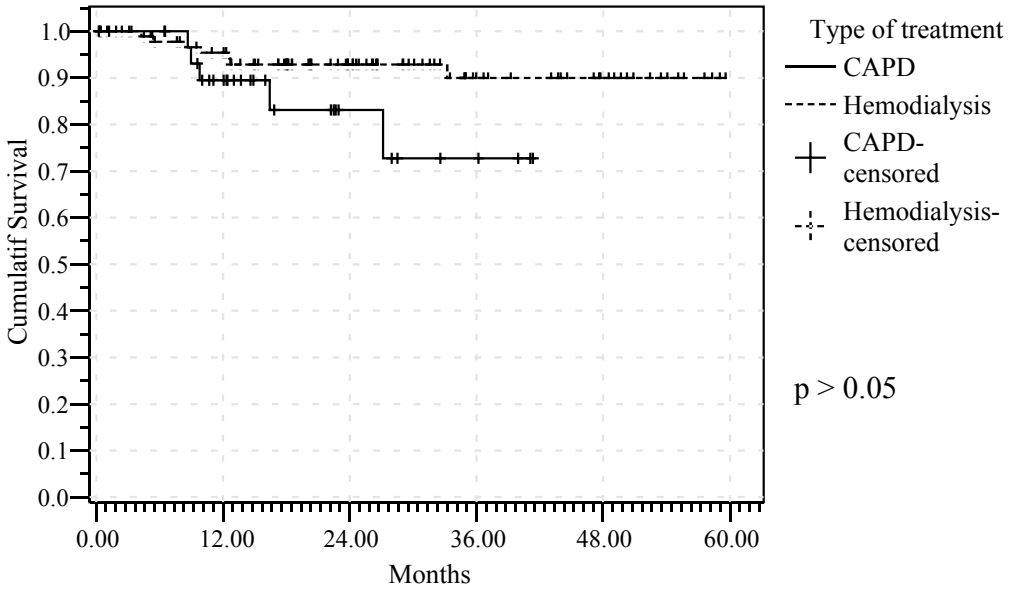

Figure 1 Survival Curve According To The Treatment

Kaplan-Meier analysis showed that there were no difference of survival rate between the two treatments (log rank: p=0.093) although during the first 10 months of observation the CAPD subjects have better survivorship (FIGURE 1) as compared to haemodialysis subjects. Factors identified (TABLE 5) influencing the survival of haemodialysis subjects were diabetes mellitus (p=0.014), albumin level (p=0.0005), creatinine level (p=0.020) and haemoglobin level (p=0.002), whereas for CAPD subjects were age of initial treatment (p=0.039), diabetes mellitus (p=0.038), CVD (0.002) and Kt/V (p=0.0005) for CAPD subjects.

Table 5 The Comparison Of Subjects By Sociodemographic Factors, Smoking, Nutritional Parameter And Kt/V For Each Treatment Group

Factors	Characteristic	Haemodialysis		CAPD	
		Mean (month)	*P* (log rank)	Mean (month)	*P* (log rank)
Sex	Male	56.53	0.295	36.63	0.966
	Female	53.34		34.44	
Age	< 50	55.24	0.821	#	**0.039**
	≥ 50	53.91		30.44	
Ethnic	Malay	55.38	0.655	35.36	0.291
	Non- Malay	53.53		25.41	
Marital status	Married	54.27	0.198	33.76	0.329
	Single	#		#	
Educational level	Primary school and less	52.01	0.933	#	0.147
	Secondary school and upper	55.07		32.51	
Income	< RM 1000	55.02	0.748	39.20	0.165
	> RM 1000	54.58		30.97	

Method of payment	Self	53.53	0.882	#	0.316
	Free/ subsidised	55.43		33.71	
Smoking	Non-smoker	54.87	0.776	32.57	0.346
	Smoker	54.86		38.85	
Diabetes mellitus	Present	41.81	**0.014**	30.13	**0.038**
	Absent	57.82		#	
Hypertension	Present	55.13	0.653	34.62	0.605
	Absent	51.48		#	
Cardiovascular disease (CVD)	Present	46.10	0.326	17.86	**0.002**
	Absent	55.84		39.33	
Body mass index (BMI)	< 23	55.10	0.485	#	0.412
	≥ 23	55.06		34.37	
Albumin (g/l)	< 35	46.48	**0.0005**	33.58	0.121
	≥ 35	#		#	
Cholesterol (mmol/l)	< 5.2	56.03	0.474	31.86	0.302
	≥ 5.2	52.07		36.87	
Triglyceride (mmol/l)	< 1.7	52.80	0.136	23.23	0.081
	≥ 1.7	58.22		37.65	
Creatinine[a] (umol/l)	< 858.4	49.58	**0.020**	31.02	0.055
	≥ 858.4	58.44		#	
Urea[a] (mmol/l)	< 18.85	53.95	0.383	34.82	0.763
	≥ 18.85	55.11		27.47	
Haemoglobin[a] (g/dl)	< 10	49.05	**0.002**	34.85	0.861
	≥ 10	#		28.55	
Kt/V	< 1.2	52.27	0.289	8.68	**0.0005**
	≥ 1.2	55.91		35.85	

The expected survival was not calculated as all subjects were censored.
[a] Categorised at median

Table 6 shows the result of Cox Proportional Hazard Regression. Factors identified to reduce the survival of haemodialysis patients were low albumin (HR 0.669, 95% CI: 0.513 - 0.873) and haemoglobin level (HR 0.403, 95% CI: 0.225 - 0.720), but there was no factor found influencing the survival of CAPD patient.

Table 6 Hazard Ratio Of Factors Studied For Haemodialysis Subjects

Factor	B	SE	Wald	dk	*p*	Hazard Ratio (Exp(B)	95.0% CI (HR)
Albumin	-0.402	0.136	8.788	1	**0.003**	0.669	0.513 – 0.873
Hb	-0.910	0.297	9.390	1	**0.002**	0.403	0.225 - 0.720

DISCUSSION

Comparative analyses have been done for haemodialysis and CAPD treatment by using χ^2–test and t-test where appropriate and also Mann-Whitney U test followed by Kaplan-Meier and Cox Proportional Hazard Regression. The total number of patients was 197, not much different compared to the local study with 217 patients. Of the 132 subjects selected, more patients received haemodialysis treatment (99 patients) compared to CAPD (33 patients), since CAPD is only available from the year 2000 at Hospital Tengku Ampuan Afzan[20].

Majority of the cause of ESRD were unknown (40.2%). However, for the known cause diabetes mellitus was the main cause of the disease (32.58%). This doesn't differ much from the study done earlier for the whole Malaysia between 2002 and 2003. Therefore effort must be

intensified towards prevention and control of diabetes mellitus[3].

Majority of the subjects were Malay (65.9%). This might be due the fact that other ethnicities tend to receive treatment from the private centre which were not included in this study. There were more male patients (59.8%) in this study even after the subjects were divided according to type of dialysis treatment given (Haemodialysis: Male 58.6%, CAPD: Male 63.6%). This may reflect the higher incidence rate and poor control of diabetes mellitus in male patients. Majority of CAPD patients (87.9%) received free treatment as compared to haemodialysis (55.6%) and the difference was statistically significant (p=0.001). But more haemodialysis patients have income of less than RM1000 per month (65.7%) as compared to CAPD (48.5%) although it was not statistically significant (p=0.079). This could be due to the majority of CAPD patients were government staff, or dependents of government staff.

The overall mortality rate for this study was 9.1%, less than the rate for Malaysia (10%) for the period of 1980 to 2003. May be it reflect the better services given by the government facilities in the state of Pahang. The mortality rate for CAPD was 15.2%, which was more than of haemodialysis patients (7.1%). This is consistent with the findings of a similar study[6]. The mortality incidence rate also higher for CAPD patients (100.10 *per 100 person years*) as compared to haemodialysis (3.26 *per 100 person years*). However the difference was not statistically significant (χ^2, p=0.174).

Kaplan-Meier analyses show a higher survival mean for haemodialysis (55 months) when compared to CAPD subjects (35 months). This occurs due to a higher mortality rate among CAPD patients, most likely due to presence of more elderly patients in the CAPD group. However there was no significant difference of survival rate between the two groups (log rank: p=0.093), although a report showed that CAPD patients have 74% higher mortality compared to haemodialysis[20]. As we can see from FIGURE 1, the survival rate changes after 10 months of treatment. The haemodialysis group have better survival rate after 10 month of treatment but CAPD patients have better survival rate earlier on.

The study also found that the presence of diabetes mellitus (p=0.014), albumin less than 35g/l (p=0.0005), creatinine of more than 858.4umol/l (p=0.020) and haemoglobin level less than 10g/dl (p=0.002) will influence the survival of haemodialysed patient. Whereas for CAPD patients, their survival was influenced by age at onset of treatment (p=0.039), the presence of diabetes mellitus (p=0.038), CVD (p=0.002) and the value of Kt/V less than 1.2 (p=0.0005).

Significant factors from the Kaplan-Meier analysis were included into the Cox Proportional Hazard Regression. For CAPD patients, none of the factors were found to be significant in the analysis. However for haemodialysis, the significant factors were albumin (p=0.003) and haemoglobin level (p=0.002).

Haemodialysis patients with higher albumin level (>35 g/l) have less mortality risk as compared to low albumin level (RR 0.669, 95% CI: 0.513-0.873). This finding is similar with other studies[3, 10 & 21].The problem of malnutrition is common in ESRD patients who receive haemodialysis treatment and the prevalence of this problem can affect up to 40% of the patients[22,23]. Several factors can cause malnutrition such as nutrient loss into the dialysate, nausea and loss of appetite, uraemia and also chronic blood loss. Albumin level is one of malnutrition parameter and is an indicator for the protein storage in the body[22]. It can change due to process of catabolism such as infection that is common in these patients.

ESRD patients who receive haemodialysis treatment and have low haemoglobin level will have higher mortality risk (RR 0.403, 95% CI: 0.225-0.720), similar to other studies[3,24]. Anaemia is common among ESRD patients and due to the complication of uraemia[25]. The relationship of anaemia and risk of mortality could be due to malnutrition and systemic inflammation that are common in these patients[24]. These factors may lead to cardiovascular failure leading to high mortality.

Limitation of the study

The main problem in conducting a study using secondary data is to obtain complete and reliable data whereby missing data is common. In this study, 33.5% of total numbers of registered subjects were not included due to incompleteness of data, the subject received different kind of dialysis modality previously or underwent a renal transplant before. 'Intention to-treat' analyses may be useful to overcome this problem but the small number of subject may hinder its usefulness.

The other problem was that only a small number of the subjects had achieved the primary end point (died: 7 for haemodialysis and 5 for CAPD), therefore it was difficult to calculate the median of the survival time or the time corresponding to a survival portion of 0.5 in the survival curve. This also contributes to the situation where all subjects were censored or no primary end point was observed for certain factors being studied. The problem may be overcome by lengthening the observation to 8 or 10 years. In addition the CAPD programme was only started at the year of 2000, thus the number of subjects that could be enrolled were limited.

CONCLUSION

Despite the limitations, 2 factors were identified as potential predictor for the survival of haemodialysis patients. A higher albumin and haemoglobin level will improve the survival by seven and four time respectively.

Albumin level is one of the nutritional status indicators and it should be maintained at a higher or adequate level to achieve better survival in haemodialysis patients. Every patient's nutritional status should be assessed continuously. Any factors affecting the patient's diet has to be looked at and the problems should be corrected. Appropriate diet counselling will ensure that they will have ample knowledge and understanding the important of good diet practice.

Anaemia is common in ESRD patients. Based on this study, a higher haemoglobin level will lead to better survival of haemodialysis patients. Currently not all patients are treated with erythropoietin to increase their haemoglobin level. Therefore this should become a standard treatment all haemodialysis patients in future, hopefully at no or little cost to them.

The most important measure to overcome this problem is prevention of the disease (ESRD) itself. As diabetes mellitus had been identified as the major cause of this disease, the prevention, early detection and control program of diabetes mellitus should be strengthened continuously. All known diabetic patients should be treated adequately to delay the progression to renal disease. To ensure a good surveillance of these patients, perhaps a notification system for diabetes mellitus should be initiated.

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