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Association Between Dialysis Dose and Biochemical Blood Parameters

(Hubungan antara Dos Dialisis dan Parameter Biokimia)

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ABTRACT

The end stage renal disease (ESRD) patients requires hemodialysis to survive. Efficacy of the treatment is determined by evaluation of minimal dialysis dose (Kt/V) which is 1.2. A cross sectional study was conducted among patients that undergo hemodialysis in a dialysis centre in Kuala Lumpur, Malaysia. The objectives of the study were to determine the association between dialysis dose and demographic factors and assessed the association between biochemical blood parameter and the demographic factors. The biochemical blood parameters were serum albumin, creatinine, cholesterol and hemoglobin. Result showed that all Indians and 54% of Chinese patients achieved the required dialysis dose. However only 29% of Malay patients attained the effective dialysis dose. More women patients accomplished the dialysis dose of at least 1.2 compared to men patients with odd ratio of 11.24. All the biochemical blood parameters were independent of the demographic factors. However, the cholesterol level was associated significantly with gender ($p<0.05$). In conclusion, the study found the biochemical blood parameter and dialysis dose were not influenced by the demographic factors.

Keywords: Biochemical blood parameters; dialysis dose; end stage renal disease; hemodialysis

ABSTRAK

Pesakit yang mengalami kegagalan renal peringkat lewat (ESRD) perlu menjalani rawatan hemodialisis untuk meneruskan kehidupan. Kerbekesanan rawatan ditentukan berdasarkan kepada dos dialisis (Kt/V) iaitu 1.2. Suatu kajian keratan rentas telah dijalankan ke atas pesakit yang menerima rawatan hemodialisis di pusat dialisis di Kuala Lumpur, Malaysia. Objektif kajian ini adalah untuk menentukan hubungan antara dos dialisis dengan faktor demografi. Kedua, kajian ini juga ingin menentukan hubungan antara parameter biokimia dan faktor demografi. Parameter biokimia adalah serum albumin, kreatinin, kolesterol dan hemoglobin. Hasil kajian menunjukkan bahawa kesemua pesakit berbangsa India dan 54% pesakit berbangsa Cina mencapai dos dialisis yang diperlukan. Walau bagaimanapun, hanya 29% pesakit berbangsa Melayu mencapai dos yang efektif. Lebih ramai pesakit wanita yang mencapai dos dialisis sekurang-kurangnya 1.2 berbanding dengan pesakit lelaki dengan nisbah odds 11.24. Kesemua parameter biokimia adalah tidak bersandar dengan faktor demografi. Walau bagaimanapun aras kolesterol mempunyai hubungan yang signifikan dengan faktor jantina ($p<0.05$). Kesimpulannya, kajian ini menunjukkan bahawa parameter biokimia dan dos dialisis tidak mempunyai perkaitan dengan faktor demografi.

Kata kunci: Dos dialisis; hemodialisis; kegagalan renal peringkat lewat; parameter biokimia

INTRODUCTION

End stage renal disease has multifactorial cause leading to temporary or permanent damage to the kidneys that results in loss of normal kidney function. The prevalence of end stage renal disease (ESRD) is high especially among older people. There are two types of treatment for ESRD patient which are hemodialysis and peritoneal dialysis (Fenton et al. 1997). In most countries especially developed country such as German, Austria, United States and Japan, urea reduction rate (URR) of at least 65% was used to identify the patients require hemodialysis (Mulder & Hillen 2001; Owen et al. 1993).

Urea reduction rate (URR) is one of the methods used to identify the hemodialysis dose. URR is described as percentage and the minimum value of URR was 65%. Previous study showed that the mortality rate for ESRD patients increased if the URR is lower than 60% (Owen et al. 1998). Other method that was used to measure the accuracy of dialysis dose was *Kt*/*V*. The minimum value for *Kt*/*V* is 1.2 (Depner 1998; Kalantar-Zadeh et al. 2003). *K* is defined as the total of dialyzer residual renal , while *t* is the period of dialysis in minutes. Meanwhile *V* is defined as the urea's volume of the hemodialysis patients (Gotch & Sargent 1985). Locatelli et al. (1998) showed that there was a negative correlation between mortality rate and dialysis dose specifically URR. This implies that the lower the dialysis dose the higher rate of mortality.

The biochemical blood parameter that is usually used to measure the accuracy of hemodialysis is serum albumin. The normal range of serum albumin is 34 until

48 g/L (Skinner 1996). Albumin is a good indicator in order to know the nutritional status of the hemodialysis patients. The nutritional factors that influence the decrease in albumin level showing that there was a relationship with higher mortality rate (Held et al. 1987; Locatelli et al. 1998). Another study by Don and Kaysen (2004), indicated that the reduction in albumin can reduce the synthesis in liver, inflammation and hypoalbuminemia. Inflamation is associated with cardiovascular disease. These findings suggest that inadequate nutrition among hemodialysis patients may be one of the factor that contribute to increase in mortality.

Apart from albumin, serum creatinine is also important as an indicator of accuracy of hemodialysis. The normal range for creatinine level was between 0.06 and 0.12 mmol/L (Horowitz et al. 1984; Spicer et al. 1999). Lowrie and Lew (1990) showed that lower levels of creatinine (less than 4 g/dL) increased mortality risk. Previous study also indicated that cholesterol level may be used as an indicator in order to measure the health status of hemodialysis (HD) patients. The normal range for the cholesterol level was less than 5.3 mmol/L (Skinner 1996). Study showed that decreased cholesterol (less than 4.5 mmol/L) and trigliseride levels will increase the mortality rate among HD patients that have cardiovascular diseases (Degoulet 1982; Liu et al. 2004).

Hemoglobin level is also an important marker for the health status among HD patients. The normal range of hemoglobin in blood is different between men and women. The normal range of hemoglobin blood for men is 13 g/dL until 18 g/dL while for women is 11.5 g/dL until 15.5 g/dL (Skinner 1996). Previous study showed that hemoglobin level lower than 10 g/dL may contribute to development of left ventricular (LV) hypertrophy. The development of LV hypertrophy may increase the mortality rate especially among ESRD patients. Chronic anemia and volume overload as well as increased cardiac work may lead to progressive enlargement of the LV and heart failure and adverse cardiovascular outcome. (Foley et al. 2000).

In this study we investigated the relationship between dialysis dose with gender, age group and ethinicity and to determine the association between the biochemical blood parameters such as hemoglobin, creatinine, cholesterol and albumin level with the demographic factors.

Methods

This was a cross-sectional study using a convenience sample of HD patients who were being dialyzed in a dialysis centre in Kuala Lumpur. The inclusion criteria were age 18 years and above, free from cardiac problem and undergoing dialysis treatment for more than 3 months and consenting to participate. The blood samples from the 46 HD patients were taken for blood test to measure the standard laboratory parameters which were serum creatinine, albumin, cholesterol and hemoglobin. The *Kt/V* was measured as a pre and post dialysis of urea samples. The post dialysis was observed 30 min after the dialysis. The calculation of *Kt/V* was done by the medical practitioner in the dialysis centre (Tattersall et al. 1996). Blood samples were taken after the dialysis and were sent to a private pathology and clinical laboratory in Kuala Lumpur to determine the serum albumin, cholesterol, creatinine and hemoglobin. The normal range of serum albumin was more than 34 mg/dL, serum cholesterol level was more than 5.3 mmol/L, serum creatinine 0.06 to 0.12 mmol/L (Harowitz et al. 1984; Spicer et al. 1999) and serum hemoglobin less than 10g/dL. Using the statistical software SPSS 17.0, chi square test and Logistic regression were used to analyse the data.

Results

Forty six patients from the dialysis centre agreed to participate in this study. They comprise of 26 men and 20 women between age of 25 and 64 years.

Table 1 shows the characteristics of participants. Standard laboratory parameters including albumin, creatinine, hemoglobin, cholesterol and the accuracy of hemodialysis treatment, *Kt/V* were measured. The results showed that most patients are Malay (54%) followed by Chinese (30%), India (7%) and other ethnic background (9%). There were more men patients (59%) than women (41%). Most of the subjects aged between 45 and 54 which was 35%, followed by age 35 until 44 (26%) and 55 until 64 (25%). HD patients aged less than 35 and over 64 were 7% each. Table 1 shows that there were 78.3% patients with the hemoglobin less than 10 g/dL. In addition, all HD patients in the dialysis centre did not have the normal range of creatinine level. As for albumin, 88% of the HD patients have normal range of albumin level (>34 g/dL) and over 50% of the patients had normal range of cholesterol level.

Association between serum albumin and hemoglobin with sociodemographic factors

Tables 2 and 3 show that there was no association between serum albumin, hemoglobin, creatinine and cholesterol with sociodemographic factors ($p>0.05$). Results on albumin level showed that about 15% of the Chinese and 4% of the Malay patients had albumin level lower than normal range. These results may suggest that Malay patients were more likely concern about their dietary intake compared to Chinese. Furthermore, patients with age over 65 and younger than 34 years have lower albumin level. This indicated that patient age between 35 and 63 were more concern about their dietary intake. Refering to hemoglobin level as an indicator, the results found that Indian men and age between 55 and 64 were more likely to have normal hemoglobin level compared to other ethnic groups, women and other age group, respectively. As for creatinine level, all the patients did not achieve the normal creatinine level, implying that the HD was not successful in assuring the creatinine level at normal range (Table 1). Apart from that, this study found that Indian ethnic group, women and aged group of 45 to 54 years old were

TABLE 1. Demographic factors and laboratory parameters of the hemodialysis patients (%)

Demographic factors	n	Percentage
Gender		
Male	27	59
Female	18	41
Age group		
25-34	3	7
35-44	12	26
45-54	16	35
55-64	12	25
>64	3	7
Race		
Malay	25	54
Chinese	14	30
Indian	3	7
Others	4	9
Hemoglobin (g/dL)		
<10g/dL	36	78.3
10-12g/dL	7	15.7
> 12g/dL	3	6
Creatinine (mmol/L)		
< 0.12mmol/l	0	0
> 0.12mmol/l	46	100
Albumin (g/L)		
< 34 g/L	6	12
≥ 34 g/L	40	88
Cholesterol (mmol/L)		
% < 5.3 mmol/l	20	44
% ≥ 5.3 mmol/l	26	56

associated with a higher cholesterol level. The result shows that there was an association between gender and cholesterol level with higher percentage of women patients with higher cholesterol level, compared to men ($p<0.05$). The reason for this higher cholesterol level may be due to atherosclerosis whereas malnutrition can caused lower cholesterol level (Avram et al. 1996; Block et al. 2004)

ASSOCIATION BETWEEN BIOCHEMICAL BLOOD PARAMETER, DIALYSIS DOSE AND SOCIODEMOGRAPHIC FACTORS

The chi-square test was also used to find the association between the blood parameters and sociodemographic factors. The results showed that there was no significant association between serum albumin level and demographic factors. Furthermore according to race, others (25%), Chinese (15%) and Malay (4%) had the albumin lower than 34 g/dL. In addition, about 8% of men and 11% of women patients also had albumin level lower than the normal range. Older age group which is more than 65 years old, and younger age group 25 to 34 years old, 34% each had lower albumin level. For the hemoglobin parameters, more than half Chinese (87%), Malay (71%) and India (67%) had hemoglobin levels less than 10 g/dL. The results also show that, there was no significant association between hemoglobin and demographic factors. The percentage of patients that had normal range of cholesterol level were 50% of each Malay and Chinese patients. Meanwhile, 66% of younger age group were between 25 to 34 years showed normal range of cholesterol level. There was no significant association between cholesterol level and other sociodemographic factors.

TABLE 2. Chi square test to find associations between serum albumin and hemoglobin with demographic factors

	Albumin < 34 g/dL	≥ 34g/dL	Hemoglobin < 10.0g/dL	≥ 10.0g/dL
Race				
Malay	4.2%	95.8%	70.8%	29.2%
Chinese	15.4%	84.6%	86.7%	13.3%
Indian	0	100%	66.7%	33.3%
Others	25%	75%	66.7%	33.3%
	$\chi^2 = 2.852$	$p > 0.05$	$\chi^2 = 1.549$	$p > 0.05$
Gender				
Male	7.7%	92.3%	66.7%	33.3%
Female	11.1%	88.9%	88.9%	11.1%
	$\chi^2 = 0.150$	$p>0.05$	$\chi^2 = 2.888$	$p > 0.05$
Age				
25-34	33.3%	66.7%	66.7%	33.3%
35-44	9.1%	90.9%	91.7%	8.3%
45-54	0	100%	75%	25%
55-64	8.3%	91.7%	58.3%	41.7%
> 65	33.3%	66.7%	100%	0
	$\chi^2 = 5.775$	$p > 0.05$	$\chi^2 = 4.392$	$p > 0.05$

*there was significance association at 5% significance level

TABLE 3. Chi square test to find the association between medical indicators and demogrphic factors

	Cholesterol	
	< 5.3 mmol/L	≥ 5.3 mmol/L
Race		
Malay	50%	50%
Chinese	50%	50%
India	0	100%
Others	33.3%	66.7%
	$\chi^2 = 2.994$	$p > 0.05$
Gender		
Male	61.5%	38.5%
Female	22.2%	77.8%
	$\chi^2 = 6.631$	$p < 0.05$ *
Age		
25-34	66.7%	33.3%
35-44	54.5%	45.5%
45-54	33.3%	66.7%
55-64	50%	50%
≥ 65	33.3%	66.7%
	$\chi^2 = 2.078$	$p > 0.05$

*there was association at 5% significance level

TABLE 4. Chi square test to find the association between medical indicator (dialysis dose) and demographic factors

	Dialysis dose	
	< 1.2	≥ 1.2
Race		
Malay	70.8%	29.2%
Chinese	46.2%	53.8%
India	0	100%
Others	100%	0
	$\chi^2 = 7.950$	$p < 0.05$*
Gender		
Male	72%	28%
Female	50%	50%
	$\chi^2 = 2.168$	$p > 0.05$
Age		
25-34	66.7%	33.3%
35-44	72.7%	27.3%
45-54	60%	40%
55-64	45.5%	54.5%
≥ 65	100%	0
	$\chi^2 = 3.727$	$p > 0.05$

For the dialysis dose *Kt/V* variable, the results showed that half of women have *Kt/V* more than 1.2. Meanwhile, from Table 4, 73% patients aged 35 to 44 almost had normal dialysis dose. There was a significant association between dialysis dose and ethnicity ($p<0.05$). The odds ratio of normal range *Kt/V* and lower dialysis dose showed that it was 3.5 times more likely patient with lower albumin (<34 g/dL) to achieve normal dialysis dose. According to Table 5, the odds ratio of patients that had hemoglobin less than 10 g/dL was 0.452 times lower compared to patients that had normal range hemoglobin in order to achieve the normal range of dialysis dose. This suggests that lower percentage of patients that have normal range of hemoglobin achieve normal *Kt/V*. Patients with higher cholesterol level had seven times higher dialysis dose compared to patients that had lower cholesterol level. Many studies have indicated that lower serum cholesterol level is associated with malnutrition and one of the factor of mortality (Avram et al. 1996; Liu et al. 2004). In this study it is shown that patients with higher cholesterol level are reflecting a higher probability to achieve the minimal range of dialysis dose, therefore it increased the survival rate of hemodialysis patients.

TABLE 5. Logistic regression for Kt/V with medical indicators

	B	SEM	p value	Odds ratio
Albumin				
< 34 g/dL	1.257	1.345	0.350	3.515
≥ 34 g/dL	–	–	–	–
Cholesterol				
< 5.3 mmol/L	1.957	1.133	0.084	7.078
≥ 5.3 mmol/L	–	–	–	–
Hemoglobin				
< 10 g/dL	- 0.795	0.765	0.299	0.452
≥ 10 g/dL	–	–	–	–
Gender				
male	- 2.415	1.143	0.035*	0.089
female	–	–	–	–

*significance at 5% significance level. The indicator of the parameter is coded as 0

Discussion

In the dialysis centre under study, majority of ESRD patients undergoing haemodialysis were Malays. Conversely, study by Abu Bakar and Zaki (1986) found that the prevalence of Chinese was highest in getting the hemodialysis treatment. High prevalence of Malays ESRD patients can be explained due to the fact that the dialysis centre was located near Malay residences. Additionally, this study found that there were more men patients compared to women which was similar to study by Held et al. (1996). This can be explained by the cause of renal failure. It is known that diabetes and hypertension are the major cause of renal failure. Renal failure occurs due to lower awareness and knowledge of the complications from diabetes and hypertension.

The dialysis dose was used to determine the effectiveness of HD. The dialysis dose can be calculated in URR or *Kt/V*. In this study, *Kt/V* was used to identify the dialysis dose. From the study we found that Indian patients are likely to have the normal range of dialysis dose (> 1.2). There was significant association between race and dialysis dose ($p<0.05$). This implies that the effective dialysis dose was higher among the the Indian subjects compared to Malays, Chinese and others ethnicity. (Fisell et al. 2004; Frankenfield et al. 1999; Owen et al. 1998).

Result from the logistic regression analysis showed that there was significant relationship between the dialysis dose and gender ($p<0.05$). This study indicated that women subject was 11.24 times more likely achieve the desired dialysis dose compare to men. This was probably because women were more likely to have higher level of awareness in nutrition by following the medical prescriptions and taking medicine in time. Study by Owen et al. 1998 showed that women patients had higher URR compared to men patients.

Previous study in North America among ESRD patients indicated that the lower hemoglobin level (<9 g/dL) may increase the risk of death by 2.11 times compared to patients that has hemoglobin level 11 until 12 g/dL (Ofsthun et al. 2003). The mechanism of lower hemoglobin and risk of death was patients that have lower hemoglobin level due to difficulty to produce eritropoeitin during the HD treatment which inevitably leads to anemia. Previous study showed that anaemia was associated with left ventricular(LV) enlargement. LV enlargement may cause heart disease and maybe death especially among ESRD patients. Consequently, it is important for the HD patients to achieve the hemoglobin target which is hemoglobin level of more than 10 g/dL (Foley et al. 2000). Normalization of hemoglobin using epoetin may improve quality of life especially among ESRD patients (Besarab et al. 1998; Drueke et al. 2006).

Prior study suggested that the decline in serum albumin may increase mortality rates (Owen et al. 1998). Serum albumin is a nutritional parameters that is usually studied among HD patients. Most of the renal disease patients had protein energy malnutrition and wasting. The mechanism of decline in serum albumin and mortality rates is maybe due to the protein metabolisme disorder, metabolic acidosis, endocrine abnormality and cardiac failure, infection and others. The lower intake of food due to uremia toxicity caused nausea and vomiting among HD patients. The dialysis procedure increased the protein catabolisme that may cause decline in protein and amino acid in inflammation reponse between patient blood and dialysis machine (Locatelli et al. 1998). The mechanism of decline in albumin may contribute to increase in the mortality rates is because the patients are malnutrition due to underdialysis or decreased in food intake (Lowrie & Lew 1990).

A study for two years has identified that mortality rates increased as the cholesterol level decrease among dialysis patients due to inflammatory or malnutrition (Liu et al. 2004). Malnutrition may also be manifested by a decrease in serum cholesterol level. A study by Chan (1995) showed that the cholesterol level among renal patients was lower compared to normal patients (Chan 1995). Degoulet et al. (1982) suggested that patients with cholesterol level 0f less than 5.3 mmol/L have an increase death risk. Cholesterol is an important component to maintain intergrity of the membrane cell.

The limitations of this study is the limited information regarding the background of the patients. It is suggested for future research to consider whether patients have diabetes, hypertension and cardiac problem. More over due to time constraint, the biochemical parameters and *Kt/V* is only measured once. It is suggested in the future to collect baseline, 3 months and 6 months in order to determine the effect of time on the biochemical parameters. Another factor that may influence the study is the time of the predialysis either morning, midday or evening. Study by Mattana et al. (1995) indicated that the biochemical parameters such as creatinine, albumin differ slightly according to the time of the beginning of the dialysis among ESRD patients.

Conclusions

The hemodialysis study involving study of demographic factors and biochemical blood parameter is important in order to determine the factors that influence dialysis dose which subsequently predicts the survival rate of the HD patients. This study provided information to medical practiotioners regarding patients that may not achieve the normal range of dialysis dose. This study suggests that the dialysis dose had associations with ethnicity. Moreover, it also suggests that women patients were more likely to achieve the normal dialysis dose. In addition, there was no significant associations between albumin, cholesterol level, blood hemoglobin with demographic factors. Moreover, the cholesterol level also had association with gender. Higher percentage of men patients were found to have cholesterol level lower than 5.3 mmol/L compared to

women. In conclusion, the dialysis dose and biochemical parameters may be influenced by other factors but not significantly influenced by demographic factors.

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