

Potential Risk Factors of End Stage Renal Disease in Patients of Hemodialysis

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Abstract: The purpose of this research is to evaluate potential risk factors and its correlation with probability of dying and frequency of hemodialysis from the first treatment among hemodialysed patients in hemodialysis center in Penang, Malaysia and Jakarta, Indonesia. A cohort prospective study was conducted in this research. Universal sampling were used to select 178 and 78 patients who had been followed for 9 months in Hemodialysis Center in Jakarta and Penang, respectively. Cox regression was used to analyze probability of dying among these patients. In HD center Jakarta, Indonesia, 47 hemodialysed patients had cardiovascular disease while 4 of 8 of those patients who had duration of having cardiovascular disease less than 5 years died during study and rest of them had duration of having cardiovascular disease more than 6 years with 95% CI 1.29-4.43, P = 0.006. In a HD center in Penang, Malaysia, 28 hemodialysed patients had cardiovascular disease and only 4 of them died during the study and all of them had duration of having cardiovascular disease more than 6 years with 95% CI 0.64-6.34, P = 0.23. In this study, only duration of having cardiovascular disease showed significant relationship with probability of dying among hemodialysed patients in Jakarta, Indonesia.

1 INTRODUCTION

According to the World Health Organization (2005), approximately 35 million people died due to chronic kidney disease (Levey *et al.*, 2007). The prevalence of End Stage Renal Disease (ESRD) in the world were more than 2 million people (Ortiz *et al.*, 2014). An adjusted 5-year survival of all patients with ESRD (treated with dialysis or transplantation) was 41% in the USA, 48% in Europe and 60% in Japan for patients with ESRD onset between 2004 and 2008 (Robinson *et al.*, 2016).

Risk factor is an alarm pointing to worst condition that may happen for CKD patients. In this case, information about risk factors on CKD is very important for others to avoid severity of ESRD. People who are not aware of the risk factors, signs and symptoms of CKD may be a victim of ESRD patients in future.

There are four categories of risk factors of end stage renal disease. They are susceptibility, initiation, progression and end-stage factors. Susceptibility factors depend on sociodemographic

variables such as age, family history and race. Initiation factors depend on the disease such as metabolic disorder, infection, autoimmune and drug toxicity, while, progression factors depend on the severity of the metabolic disorder such as the higher blood pressure, higher proteinuria and poor glycemic control and End-stage factors depend on lack of attention to the progression factors such as lower dialysis dose and high serum phosphorus (Levey, A.S., Eckardt, K., Tsukamoto, Y., Levin, A., Coresh, J., Rossert, J., de Zeeuw, D., Hostetter, T., Lameire, N., Eknoyan et al., 2005).

2 MATERIAL AND METHODS

Research was carried out in hemodialysis (HD) ward Jakarta, Indonesia and Pulau Pinang, Malaysia. Universal sampling were used to select 178 and 78 patients who had been followed for 9 months in Hemodialysis Center Jakarta and Penang, respectively. A cohort prospective study was conducted in this research.

Table 1: Potential Risk Factors of ESRD and Probability of Dying Among Hypertensive/Diabetic Patients Who Undergone Hemodialysis (Prospective Sample / 9 Months Followed up)

Potential Risk Factors	B		Exp (B) Hazard Ratio		95% CI For Exp (B)		P * Value	
	Jakarta, Indonesia	Penang, Malaysia	Jakarta, Indonesia	Penang, Malaysia	Jakarta, Indonesia	Penang, Malaysia	Jakarta, Indonesia	Penang, Malaysia
Cause of ESRD	0.49	2.02	1.64	7.53	0.75-3.58	0.66-85.58	0.22	0.10
Duration of having CKD	-3.24	-1.23	0.04	0.29	0.001-1.85	0.06-1.37	0.10	0.12
Duration of having CVD	0.87	0.70	2.39	2.01	1.29-4.43	0.64-6.34	0.006*	0.23
Duration of having HT	-0.24	-0.67	0.79	0.51	0.45-1.39	0.16-1.63	0.41	0.26
Duration of having DM	-0.38	0.43	0.69	1.53	0.43-1.11	0.89-2.64	0.12	0.13

Before requesting for the ethical approval, researcher had a good clinical practice certificate. Ethical clearance were sourced from ethical medical committee from Faculty of Medicine in Indonesia (728/UN2.F1/ETIK/2015) and Clinical Research Center Pulau Pinang Hospital Malaysia ((5)KKM/NIHSEC/P16-133). The approval letters were given before starting data collection.

The collection of data also started after determining the inclusion criteria and patients also signed the agreement. The study included diabetic and / hypertensive patients who undergone hemodialysis and have aged more than 18 years old. Patients who have cancer, HIV/AIDS, Systemic Lupus Erythema and pregnant were excluded in this study. All the data were transferred to the clinical data collection form.

3 RESULTS

Table 1. shows correlation between potential risk factors of ESRD and probability of dying in both HD centers. Probability of dying can be measured by these potential risk factors in this study, but only duration of cardiovascular disease showed significant relationship with probability of dying in HD center Jakarta, Indonesia as shown in Table 1.

Cause of ESRD increased risk of death almost 2 times among hemodialysed patients in a HD center in Jakarta, Indonesia and it also increased risk of

death more than 7 times among hemodialysed patients in a HD center in Penang, Malaysia anytime during 9 months followed up and P value for both indicated no statistical difference as shown in Table 1.

Duration of having cardiovascular disease elevated risk of death more than 2 times in both HD center in Jakarta, Indonesia and Penang, Malaysia anytime during the 9 months followed up but only patients of hemodialysis in Jakarta, Indonesia who showed significant relationship.

3.1 Cause of ESRD

Cause of ESRD is one of the potential risk factors which can influence duration of hemodialysis among hemodialysed patients (Disease and Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group, 2012). Table 3 shows correlation between potential risk factors of ESRD and frequency of HD from first time on HD in both HD center Jakarta, Indonesia and Penang, Malaysia.

Significant correlation was found among hemodialysed patients in Penang, Malaysia. It can be seen from median value for each group, while the significant difference of duration of hemodialysis for each group based on cause of ESRD was shown. Hemodialysed patients who had hypertension had the highest median (1062) value compared with hemodialysed patients who had diabetic mellitus and DM & HT in a HD center Penang, Malaysia as shown in Table 2.

Table 2. Cause of ESRD and Frequency of HD from first time on HD

	N for each group of cause of ESRD	Median for each group (Times of HD Frequency)	P*
Frequency of HD from first time on HD (Indonesia)	DM (33)	127	0.36
	HT (98)	135	
	DM & HT (47)	146	
Frequency of HD from first time on HD (Malaysia)	DM (5)	238	0.001*
	HT (43)	1062	
	DM & HT (30)	624.5	

* *A Kruskal-Wallis Tests*

Table 3. Duration of having CKD and Frequency of HD from first time on HD Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis

Component	Years (N) Duration of having CKD	Median for each group (Times of HD Frequency)	P*
Frequency of HD from first time on HD (Indonesia)	≤ 5 years (153)	127	< 0.001*
	≥ 6-10 years (20)	598	
	≥ 11-15 years (5)	1137	
Frequency of HD from first time on HD (Malaysia)	≤ 5 years (36)	291	< 0.001*
	≥ 6-10 years (24)	1008	
	≥ 11-15 years (9)	1821	
	≥ 16-20 years (9)	2566	

* *A Kruskal-Wallis Test*

Table 4. Duration of Having Cardiovascular Disease and Frequency of HD Since First HD Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis

Component	N for each group of duration of having cardiovascular disease Years (N)	Median for each group (Times of HD Frequency)	P*
Frequency of HD Since First HD (Indonesia)	≤ 5 years (41)	127	0.21
	≥ 6 years (6)	280.5	
Frequency of HD Since First HD (Malaysia)	≤ 5 years (12)	659	0.005*
	≥ 6 years (20)	1530	

* *A Kruskal-Wallis Test*

3.2 Duration of having CKD

Duration of ESRD may affect the duration of hemodialysis among hemodialysed patients (Disease and Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group, 2012). Table 3. shows correlation between duration of having CKD and frequency of HD from first time on HD in both HD centers Jakarta, Indonesia and Penang, Malaysia.

Significant correlation between duration of having CKD and frequency of HD from first time on HD were found among hemodialysed patients in both HD centers as shown in Table 3. In Indonesia, the highest median value (1137 times) of frequency of HD from first time on HD was shown by the third group (≥ 11-15 years) of duration of having CKD. However, in Malaysia, median value of 2566 times was shown by fourth group (≥ 16-20 years) of duration of having CKD.

Table 5. Duration of Having Hypertension and Frequency of HD Since First HD Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis

Component	N for each group Years (N) of duration of having hypertension	Median for each group (Times of HD Frequency)	P*
Frequency of HD Since First HD (Indonesia)	≤ 5 years (117)	125	<0.001*
	≥ 6-10 years (34)	401.5	
	≥ 11-15 years (14)	447.5	
	≥ 16-20 years (6)	225	
	≥ 21 years (7)	197	
Frequency of HD Since First HD (Malaysia)	≤ 5 years (6)	208.5	<0.001*
	≥ 6-10 years (26)	636.5	
	≥ 11-15 years (20)	966.5	
	≥ 16-20 years (13)	1665	
	≥ 21 years (13)	1542	

*Kruskal Wallis Test

Table 6. Duration of Having Diabetes Mellitus and Frequency of HD Since First HD Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis

Component	N for each group of duration of having diabetes mellitus	Median for each group (times of HD Frequency)	P*
Frequency of HD Since First HD (Indonesia)	≤ 5 years (26)	135	0.74
	≥ 6-10 years (22)	126	
	≥ 11-15 years (17)	172	
	≥ 16-20 years (8)	228.5	
	≥ 21 years (9)	141	
Frequency of HD Since First HD (Malaysia)	≤ 5 years (5)	240	0.01*
	≥ 6-10 years (8)	475	
	≥ 11-15 years (11)	802	
	≥ 16-20 years (5)	565	
	≥ 21 years (6)	888.5	

*A Kruskal-Wallis Tests

3.3 Duration of Having Cardiovascular Disease

Duration of having cardiovascular disease may influence the duration of hemodialysis among hemodialysed patients (Ortiz *et al.*, 2014). Table 5. shows correlation between duration of having cardiovascular disease and frequency of HD from first time on HD in both HD center Jakarta, Indonesia and Penang, Malaysia.

Significant correlation ($p = 0.005$) between duration of having cardiovascular disease and frequency of HD from first time on HD was found among hemodialysed patients in a HD center Penang, Malaysia as shown in Table 4.

Duration of having hypertension and frequency of HD since first HD were found significant among hemodialysed patients in both HD centers of Malaysia ($P < 0.001$) and Indonesia ($P < 0.001$) as shown in Table 5. In Indonesia, the highest median

value of frequency (447.5 times) of HD from first time on HD was shown by the third group ($\geq 11-15$ years) of duration of hypertensive patients. However, in Malaysia, patients with $\geq 16-20$ years duration showed frequency of 1665 times in hypertensive patients.

3.4 Duration of Having Diabetes Mellitus

Duration of having diabetes Mellitus may affect the duration of hemodialysis among hemodialysed patients. Table 6 shows correlation between duration of having diabetes mellitus and frequency of HD from first time on HD in both HD center Jakarta, Indonesia and Penang, Malaysia.

Significant correlation between duration of having diabetes mellitus and frequency of HD since first HD was found among hemodialysed patients in a HD center Penang, Malaysia as shown in Table 6.

4 DISCUSSION

In Penang, Malaysia, all these five potential risk factors (cause of ESRD, duration of having CKD, duration of having cardiovascular disease, duration of having hypertension and duration of having diabetic mellitus) showed significant correlation with frequency of HD from first treatment. Meanwhile, only two potential risk factors showed significant relationship in HD center Jakarta, Indonesia including duration of having CKD and duration of having hypertension.

Duration of having CKD was dependent on frequency of hemodialysis since first treatment. Duration of having CKD was calculated by how many session (frequency) of hemodialysis, which had been done by those patients. It is the same with duration of cardiovascular, hypertensive and diabetic among those patients. Length of duration these diseases will be equal to frequency of hemodialysis because those diseases can not be excluded permanently.. Agarwal, 2005 reported that the use of antihypertensive drugs treatment improve survival (Agarwal, 2005).

In this finding, frequency of hemodialysis among diabetic and / hypertensive patients influenced duration of having CKD and duration of having hypertension in both HD centers. Some studies identified that increasing dialysis time and frequency affect hypertensive condition (Fagugli *et al.*, 2001, 2006; Culleton *et al.*, 2007).

Many factors contributed length of hemodialysis session, some of them are good medication and less of complication. Chandrashekar *et al.*, 2014 reported that there is no significant difference in terms of survival among diabetics compared with non-diabetics (Chandrashekar, Ramakrishnan and Rangarajan, 2014). Another study revealed that the survival of patients on hemodialysis with diabetes mellitus was lower than those patients without diabetes mellitus (Ghaderian *et al.*, 2015).

In Australia, New Zealand and the United States, Cardiovascular Disease (CVD) was reported as the leading cause of death in dialysis patients (Annual Data Report Minneapolis, 2006; McDonald, 2015). Another study, Mailloux *et al.*, 1991 identified the causes of death in maintenance dialysis patients who survived at least 90 days and were monitored during a 16 year period and cardiovascular disease was one of the causes of death among those patients (Mailloux *et al.*, 1991).

Cardiovascular disease is one of the complications of end-stage renal failure (Marry Anne and Alledredge, 2013). The statement about

correlation of CV in presence of CKD is still a controversy (Herzog *et al.*, 2011). In this study, duration of cardiovascular disease influenced the probability of dying / risk of mortality among hemodialysed patients in a HD center Jakarta, Indonesia.

5 CONCLUSION

Five potential risk factors of ESRD were found in this study: cause of ESRD, duration of having CKD, duration of having cardiovascular disease, duration of having hypertension and duration of having diabetes mellitus. Only duration of having cardiovascular disease showed significant relationship with probability of dying but only in HD patients in Jakarta, Indonesia; whereas duration of having cardiovascular disease elevated risk of death more than 2 times in both HD centers in Jakarta, Indonesia and Penang, Malaysia.

6 DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST AND ACKNOWLEDGEMENT

The authors declared that we have no conflict of interest.

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