

**THERAPEUTIC OUTCOMES AND MORTALITY  
RELATED TO HEMODIALYSIS AMONG  
HOSPITALIZED HYPERTENSIVE AND  
DIABETIC PATIENTS IN JAKARTA, INDONESIA  
AND PENANG, MALAYSIA**

**DIANA LAILA RAMATILLAH**

**UNIVERSITI SAINS MALAYSIA**

**2018**

**THERAPEUTIC OUTCOMES AND MORTALITY  
RELATED TO HEMODIALYSIS AMONG  
HOSPITALIZED HYPERTENSIVE AND  
DIABETIC PATIENTS IN JAKARTA, INDONESIA  
AND PENANG, MALAYSIA**

by

**DIANA LAILA RAMATILLAH**

**Thesis submitted in fulfillment of the requirements  
for the degree of  
Doctor of Philosophy**

**July 2018**

## ACKNOWLEDGEMENT

I would like to gratitude for all the people that supported me until finished this thesis. First of all I would like to express my appreciation and gratitude to my main supervisor Professor Dr. Syed Azhar Syed Sulaiman and my co-supervisor Dr. Amer Hayat Khan for their guidance, advice, social also moral support, and willingness to spend time in spite of their busy schedule for discussion throughout the study.

I would also like to thank to Prof. Dr. HMS Markum, SPPD, KGH Cempaka Putih Islamic hospital Jakarta and Dato' Dr. Ong Loke Meng Hospital Pulau Pinang, Malaysia where this study conducted as my field supervisors for their guidance, advice and help during data collection period.

I would also like to thanks all my colleagues and friends especially Hajia Mairo Ipadeola, Dr. Aprilita Rinayanti and Kashif Ullah Khan that always share knowledge and support me during the study. Deepest thanks and love to my family members, my mother (alm) and my father (alm) who passed away in 2017 when I completed my thesis and also thanks to my sister Riani Laili Rahmani, SH and my aunt (dr.Ihsanil Husna, Sp.Pd) for their support, courage, and for always pray for me and believing on me.

My gratitude and sincere thanks to my university, Universiti 17 Agustus 1945 Jakarta. I appreciate the head of foundation (Mr. Rudyono Darsono), rector (Dr. Virgo Simamora, MBA), vice rector (Mr. Rajesh Khana, MSc (comp)), Former Dean Pharmacy Faculty (Dr. Hasan Rachmat M,DEA, Apt) and Directur (Mr. Stefanus Lukas, MARS, Apt) for allow me to pursue my PhD. My gratitude to School of pharmaceutical sciences (USM), Institute of Postgraduate Studies (IPS-

USM) and special thanks to Prof. Dr. Nordin Razak, a statistician in IPS USM, who always helped me during my research.

Above all, all praises to Allah SWT, The Most Merciful and The Most Gracious that always gives hope and best way to me even in my hardest situations. May Allah SWT bless all the people and who support me always.

**Diana Laila Ramatillah**

## TABLE OF CONTENTS

Acknowledgement.....	ii
Table of Contents.....	iv
List of Tables.....	viii
List of Figures.....	xx
List of Abbreviations.....	xxii
Abstrak.....	xxiv
Abstract.....	xxvi
<b>CHAPTER 1 INTRODUCTION.....</b>	<b>1</b>
1.1 Introduction.....	1
1.1 Prevalence of Mortality of Hemodialysed patients in the World.....	5
1.3 Prevalence of Mortality of Hemodialysed patients in Indonesia.....	5
1.4 Prevalence of Mortality of Hemodialysed patients in Malaysia.....	6
1.2 Therapeutic Outcomes of Hemodialysed patients.....	6
1.3 Research Question.....	8
1.4 Rationale of the study.....	8
1.5 Significant of the study.....	9
1.6 Objectives.....	10
1.6.1 General Objective.....	10
1.6.2 Specific Objectives.....	10
<b>CHAPTER 2 LITERATURE REVIEW.....</b>	<b>12</b>
2.1 Hemodialysis.....	12
2.2 Background progression of CKD to ESRD.....	12
2.1.1 Identification of CKD Progression.....	13
2.2.2 Risk Factors of CKD.....	15
2.2.3 CKD Signs and Symptoms.....	16
2.2.4 Comorbidities of CKD.....	18
2.3 Baseline Assessments for Hemodialysis.....	24
2.3.1 Calculating Clearance Creatinine (Clcr).....	25
2.3.2 Monitoring of Patients on Hemodialysis.....	25

2.4	Clinical Practice Pattern of Hemodialysis .....	26
2.5	Management of Complications of ESRD Among Hemodialysed patients ....	29
2.6	Quality of Life Patients on Hemodialysis .....	35
2.7	Risk Factors that Contribute to Mortality Among Hemodialysed Patients ...	36
2.8	Hemodialysis in Indonesia .....	40
2.8.1	The Incidences and Prevalence ESRD in Indonesia .....	40
2.8.2	Mortality of Hemodialysed patients in Indonesia .....	43
2.9	Hemodialysis in Malaysia.....	43
2.9.1	The Incidences and Prevalence ESRD in Malaysia.....	43
2.9.2	Mortality of Hemodialysed patients in Malaysia.....	46
<b>CHAPTER 3 RESEARCH METHODOLOGY.....</b>		<b>47</b>
3.1	Background of Study Location .....	47
3.2	Ethical Approval of the Study.....	47
3.3	Study Population and Sample .....	48
3.4	Inclusion and Exclusion Criteria.....	48
3.4.1	Inclusion Criteria .....	48
3.4.2	Exclusion Criteria .....	48
3.5	Study Design .....	49
3.6	Sampling Method.....	49
3.7	Sample Size Calculation .....	50
3.8	Research Instrument.....	50
3.9	Data Collection .....	51
3.10	Data entry and statistical analysis .....	51
3.11	Data Analysis .....	52
3.11.1	Evaluation of Demographic Data and Practice Pattern .....	52
3.11.2	Assessment of Health Related Quality of Life Hemodialysed patients .....	52
3.11.3	Evaluation of the Potential Risk Factors Of ESRD.....	54
3.11.4	Evaluation the Differences of Pharmacotherapy Between Indonesia and Malaysia .....	54
3.11.5	Potential Complications, Survival Analysis and Mortality Rate.....	55
<b>CHAPTER 4 RESULTS.....</b>		<b>57</b>
4.1	Sociodemographic Data and Practice Pattern Among Hemodialysed	

Patients in HD center Jakarta, Indonesia and Penang, Malaysia .....	57
4.1.1 Sociodemographic Data of Patients and Clinical Outcome .....	57
4.1.2 The Practice Pattern that Correlates with the Clinical Outcome Among Hypertensive and Diabetic Patients who Undergone Hemodialysis for Both HD Centers Jakarta, Indonesia and Penang, Malaysia .....	67
4.2 Assessment of the health-related quality of life (HRQOL) patients using KDQoL-SF24 Tool .....	73
4.2.1 Scoring of KDQOL-SF24 .....	75
4.3 Evaluate the Potential Risk Factors of ESRD that Correlates with the Clinical Outcome Among Hypertensive and Diabetic Patients on Hemodialysis Between Two Countries.....	97
4.3.1 Cause of ESRD .....	101
4.3.2 Duration of ESRD .....	102
4.3.3 Duration of Cardiovascular Disease .....	104
4.3.4 Duration of Hypertension .....	105
4.3.6 Duration of Diabetes Mellitus.....	106
4.4 Evaluate the differences of pharmacotherapy in ESRD patients who undergo hemodialysis between the two countries. ....	107
4.4.1 Supplement to prevent from loss of Calcium .....	115
4.4.2 Rhu-EPO (Erythropoetin Recombinant/EPO) / Anemia Medication .	119
4.4.3 Antihypertensive Drugs .....	126
4.4.4 Antidiabetic Drugs .....	133
4.4.5 Cardiovascular Drugs.....	137
4.4.6 Antiplatelet Drugs .....	141
4.4.7 Dyslipidemia Drugs .....	144
4.5 Complications among ESRD patients undergoing hemodialysis and the mortality rate and survival analysis in both Indonesia and Malaysia ....	148
4.5.1 Potential Complications .....	148
4.5.2 Survival Analysis .....	175
4.5.3 Mortality Rate .....	179
<b>CHAPTER 5 DISCUSSION .....</b>	<b>187</b>
5.1 Demographic Data, Practice Pattern and The Correlation with	

Clinical Outcome .....	187
5.2 Assessment Health Related Quality of Life.....	192
5.3 Correlation Between Potential Risk Factors and Clinical Outcome .....	196
5.4 Differences of Pharmacotherapy in Both HD Centers.....	199
5.5 Potential Complication, Mortality Rate and Survival Analysis.....	205
<b>CHAPTER 6 CONCLUSION AND SUGGESTION.....</b>	<b>220</b>
6.1 Conclusion .....	220
6.2 Limitation of This Study .....	221
6.3 Future Recommendations .....	221
<b>REFERENCES</b>	



## LIST OF TABLES

		<b>Page</b>
Table 2.1	Classification of Chronic Kidney Disease by GFR Category*	14
Table 2.2	Classification of Chronic Kidney Disease by Albumin Category*	15
Table 2.3	Risk Factors for CKD*	16
Table 2.4	Symptoms and Signs of CKD*	17
Table 2.5	Drug Therapies and Dosing Recommendations for Dialysis Patients*	21
Table 2.6	The Monitoring of Hemodialysis Process*	26
Table 2.7	Duration and Frequency of Hemodialysis by KDOQI Clinical Practice Guideline Hemodialysis Update *	28
Table 2.8	BP targeted based on KDIGO clinical practice (KDIGO, 2012a)	33
Table 2.9	Factors that Reduce Risk of Death in Dialysis Patients*	39
Table 2.10	Distribution of Gender for Hemodialysed patients from 2007 to 2012 in Indonesia*	40
Table 2.11	Distribution of Age for Hemodialysed patients in 2012 in Indonesia*	41
Table 2.12	The Percentage of AKI, ARF and ESRD Patient in 2012 in Indonesia*	41
Table 2.13	The Etiology Related to Hemodialysed Patients in 2012 in Indonesia*	42
Table 2.14	The Causes of Mortality Among Indonesian Patients on Hemodialysis in 2012*	42
Table 2.15	Stock-Flow of Renal Replacement Therapy in Malaysia from 2007 to 2012*	43

Table 2.16	Dialysis Treatment Rate by Gender Population per million in 44 Malaysia from 2007 to 2012*	44
Table 2.17	Dialysis Treatment Rate by Age Group Population in Malaysia 44 from 2007 to 2012*	
Table 2.18	Primary Renal Disease in Malaysia from 2007 to 2012*	45
Table 2.19	Cause of death on dialysis in Malaysia from 2006 to 2012*	46
Table 3.1	Reliability Analysis	53
Table 4.1	Sociodemographic Data of Hemodialysed Patients Who Had Been 58 Followed up for 9 Months in Both HD Center, Jakarta, Indonesia and Penang, Malaysia	
Table 4.2	Sociodemographic Hemodialysed Patients Who Died Since Last 5 59 Years in Both HD Center, Jakarta, Indonesia and Penang, Malaysia	
Table 4.3	Clinical Outcome Based on Sociodemographic Data of 61 Hemodialysed Patients Who Had Been Followed-up for 9 months	
Table 4.4	Month's Life Based on Demographic Data of Diabetic and/ 63 Hypertensive Patients Who Underwent Hemodialysis for Patients Who Died in Last 5 years in HD center Jakarta, Indonesia	
Table 4.5	Month's Life Based on Demographic Data of Diabetic and/ 65 Hypertensive Patients Who Underwent Hemodialysis for Patients Who Died in Last 5 years in HD center Penang, Malaysia	
Table 4.6	Probability of Dying Based on Survival Studies on 66 Sociodemographic Data Among Hypertensive/Diabetic Patients Who Undergone Hemodialysis (Prospective Sample/9 Months Followed up) in a HD Center Jakarta, Indonesia and Penang, Malaysia	
Table 4.7	Practice Pattern for Hemodialysed patients Who Undergone 69 Hemodialysis in a Hemodialysis Centre, Jakarta, Indonesia, and Penang, Malaysia	

Table 4.8	Types of Adverse Events and Side Effects of Hemodialysis Which Occurred Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis During 9 Months Followed-up and the Clinical Outcome in Both Hemodialysis Centers, Jakarta, Indonesia and Penang, Malaysia	70
Table 4.9	The Number of Hemodialysed patients Who Had Edema During Hemodialysis and the Clinical Outcome Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis in Both HD Center Jakarta, Indonesia and Penang, Malaysia	71
Table 4.10	The Number of Hemodialysed patients Who Had Hepatitis C and the Clinical Outcome Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis in Both HD Center Jakarta, Indonesia and Penang, Malaysia	72
Table 4.11	The Number of Hemodialysed patients Who Had Hyperparathyroidism and the Clinical Outcome Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis in Both HD Center Jakarta, Indonesia and Penang, Malaysia	73
Table 4.12	The Number of Hemodialysed patients Who Did Parathyroidectomy and the Clinical Outcome Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis in Both HD Center Jakarta, Indonesia and Penang, Malaysia	73
Table 4.13	Scoring of KDQOL-SF24 Questionnaire for Indonesian Patients and Malaysian Patients	76
Table 4.14	KDQoL-SF24 Scores for Each Component Based on Gender Among Hemodialysis Patients in HD Centre Jakarta, Indonesia and Penang, Malaysia	78
Table 4.15	KDQoL-SF24 Score for Each Component Based on Age Among Hemodialysed patients in a HD Center Jakarta, Indonesia and Penang, Malaysia	82
Table 4.16	KDQoL-SF24 Scores for Each Component Based on Race Among Hemodialysed patients in a HD Center Penang, Malaysia	89
Table 4.17	Scoring of Overall Health Rating by KDQoL-SF24 tool Based on Clinical Outcome in HD Center Jakarta, Indonesia and Penang, Malaysia	93

Table 4.18	Scoring Overall Health Rating by KDQoL-SF24 Tool Based on 93 Gender
Table 4.19	Scoring Overall Health Rating by KDQoL-SF24 Tool Based on 94 Age
Table 4.20	Clinical Outcome Based on Potential Risk Factors of ESRD 96 Among Hypertensive and Diabetic Patients Who Undergone Hemodialysis (for prospective sample / 9 Months followed up) in both HD center, Jakarta, Indonesia, and Penang, Malaysia
Table 4.21	Potential Risk Factors of ESRD and Probability of Dying Among 98 Hypertensive/Diabetic Patients Who Undergone Hemodialysis (Prospective Sample / 9 Months Followed up)
Table 4.22	Cause of ESRD and Frequency of HD from first time on HD 100 Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis (for prospective sample / 9 months followed up) in Both HD Center Jakarta, Indonesia and Penang, Malaysia
Table 4.23	Duration of CKD and Frequency of HD from first time on HD 101 Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis (for prospective sample / 9 months followed up) in Both HD Center Jakarta, Indonesia and Penang, Malaysia
Table 4.24	Duration of Cardiovascular Disease and Frequency of HD Since 102 First HD Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis (for prospective sample /9 months followed up) in Both HD Center Jakarta, Indonesia and Penang, Malaysia
Table 4.25	Duration of Hypertension and Frequency of HD Since First HD 103 Among Diabetic/Hypertensive Patients Who Undergone Hemodialysis (for prospective sample / 9 months followed up) in Both HD Center Jakarta, Indonesia and Penang, Malaysia
Table 4.26	Duration of Diabetes Mellitus and Frequency of HD Since First 104 HD Among Diabetic/Hypertensive Patients Who

	Undergone Hemodialysis (for prospective sample / 9 months followed up) in Both HD Center Jakarta, Indonesia and Penang, Malaysia	
Table 4.27	Medications Used by Diabetic/Hypertensive Patients Who Undergone Hemodialysis (for prospective sample / 9 Months followed up) in a Hemodialysis Centre, Jakarta, Indonesia, and Penang, Malaysia	105
Table 4.28	List of The Drugs That Patients Used During Treatment in Both HD Center, Jakarta, Indonesia And Penang, Malaysia (for prospective sample / 9 months followed up).	107
Table 4.29	Laboratory Value of Hemodialysed Patients (for prospective sample/ 9 months followed up) in a Hemodialysis Center, Penang, Malaysia	110
Table 4.30	Frequency of HD Since First HD, Calcium baseline, Calcium first followed-up and Calcium second followed-up Based on Supplement used (for prospective sample / 9 months followed up) in a HD center Penang, Malaysia	112
Table 4.31	Calcium (baseline, first followed up, second followed up) and Duration of Hemodialysis (year) Among Hemodialysed Patients (9 months followed up patients) in a Hemodialysis Center Penang, Malaysia	113
Table 4.32	Calcium Baseline and Calcium Second Followed Up Among 9 Months Followed-up Patients in a Hemodialysis Center Penang, Malaysia	114
Table 4.33	Mean and Standard Deviation of Calcium Baseline, Calcium Second Followed-up and Calcium Third Followed-up Among 9 Months Followed-up of Hemodialysed Patients in a Hemodialysis Center Penang, Malaysia	115
Table 4.34	Hemoglobin (baseline, first followed up, second followed up) and Duration of Hemodialysis (year) Among Hemodialysed Patients (9 months followed-up patients) in a Hemodialysis Center Penang, Malaysia	116
Table 4.35	Anemia and Month's Life Since First Time on HD Among Hemodialysed Patients (last 5 years' patients) in a HD Center Jakarta, Indonesia	117
Table 4.36	The Number of Hemodialysed Patients Who Had Anemia before death Since First time on HD in a HD Center, Jakarta, Indonesia	118

Table 4.37	Frequency of HD Since First HD Based on Erythropoietin Recombinant Used Among Diabetic and/ Hypertensive Patients Who Undergone Hemodialysis (9 months followed-up patients) in a HD Center Jakarta, Indonesia	118
Table 4.38	Erythropoietin Recombinant and Hemoglobin (Hgb) Laboratory Value Among Hemodialysed Patients (9 months followed-up patients) in a HD Centre Penang, Malaysia	119
Table 4.39	Hgb Baseline and Hgb Second Followed-up Among Hemodialysed Patients (9 months followed-up patients) in a Hemodialysis Center Penang, Malaysia	120
Table 4.40	Corelation of Hgb Baseline with Hgb Second Followed-up, MCV Baseline with MCV Second Followed-up and MCH Baseline with MCH Second Followed-up Among Hemodialysed Patients in a Hemodialysis Center Jakarta, Indonesia, and Penang, Malaysia	121
Table 4.41	Frequency of HD Since First HD Based on Anemia Supplement Used Among 9 Months Followed-up Patients in a HD Center Jakarta, Indonesia	121
Table 4.42	Clinical Outcome Based on Antihypertensive Used Among Hemodialysed Patients Who Had Been Followed-up for 9 Months in a HD Center Jakarta, Indonesia	122
Table 4.43	Complication, Mortality and Survival Rate Hemodialysed Patients Who Used Amlodipin and Perindopril for Patients Who Had Been Followed-up for 9 Months in a HD Both Centers Jakarta, Indonesia and Penang, Malaysia	123
Table 4.44	Frequency of HD Since First HD Based on Antihypertensive and Amlodipine Used Among 9 Months Followed-up Hemodialysed Patients in a HD center Jakarta, Indonesia, And Penang, Malaysia	124
Table 4.45	Triglyceride and HDL-cholesterol Value Based on Amlodipine used Among 9 Months Followed-up Hemodialysed Patients in a HD Center, Penang, Malaysia	125
Table 4.46	Total Cholesterol and LDL-Cholesterol Value Based on Amlodipine Used Among 9 Months Followed-up Hemodialysed Patients in a HD Center, Penang, Malaysia	126

Table 4.47	Triglyceride and HDL-cholesterol Value Based on Perindopril Used among 9 months followed up hemodialysed patients in a HD center, Penang, Malaysia	127
Table 4.48	Total Cholesterol and LDL-Cholesterol Used Based on Perindopril Used among 9 months followed up hemodialysed patients in a HD center, Penang, Malaysia	128
Table 4.49	Frequency of HD Since First HD Based on Antidiabetic Used Among 9 Months Followed-up Among Hemodialysed Patients in a HD Center Penang, Malaysia	129
Table 4.50	FBS (baseline, first followed-up, second followed-up) Hemodialysed Patients Who Died During 9 Months Followed-up in HD Center Penang, Malaysia	129
Table 4.51	FBS (baseline, first followed-up, second followed-up) Value Based on Frequency of HD From first time on HD Among 9 Months Followed-up of Hemodialysed Patients in a Hemodialysis Center Penang, Malaysia	130
Table 4.52	FBS (baseline, first followed-up, second followed-up) Value Based on Duration of Hemodialysis Among 9 Months followed up of Hemodialysed Patients in a Hemodialysis Center Penang, Malaysia	131
Table 4.53	Frequency of HD Since First HD Based on Cardiovascular Drugs Used Among 9 months followed up of Hemodialysed patients in a HD center Jakarta, Indonesia, and Penang, Malaysia	133
Table 4.54	Complication, Mortality and Survival Rate Hemodialysed Patients Who Used Nitroglycerin for Patients Who Had Been Followed-up for 9 Months in a HD Center Jakarta, Indonesia	134
Table 4.55	Total Cholesterol and LDL-Cholesterol Value Based on Cardiovascular Drugs Used Among 9 Months Followed up of Hemodialysed patients in a HD center, Penang, Malaysia	135
Table 4.56	Triglyceride and HDL-Cholesterol Value Based on Cardiovascular Drugs Used Among 9 Months Followed-up Hemodialysed Patients in a HD Center, Penang, Malaysia	136

Table 4.57	Frequency of HD Since First HD Based on Antiplatelet Used Among 9 Months Followed-up of Hemodialysed Patients in a HD Center Jakarta, Indonesia, and Penang, Malaysia	137
Table 4.58	Platelet Laboratory Value Based on Antiplatelet Drugs Used Among 9 Months Followed-up of Hemodialysed Patients in a HD center, Penang, Malaysia	137
Table 4.59	Platelet Baseline and Platelet Second Followed-up Among 9 Months Followed-up Hemodialysed Patients in a Hemodialysis Center Penang, Malaysia	138
Table 4.60	Frequency of HD Since First HD Based on Dyslipidemia Drugs Used Among 9 Months Followed-up Hemodialysed Patients in a HD Center Jakarta, Indonesia, and Penang, Malaysia	139
Table 4.61	Triglyceride and HDL-Cholesterol Value Based on Dyslipidemia Drugs Used Among 9 Months Followed-up of Hemodialysed Patients in a HD Center, Penang, Malaysia	140
Table 4.62	Total Cholesterol and LDL-Cholesterol Value Based on Dyslipidemia Drugs Used Among 9 Months Followed-up Hemodialysed Patients in a HD Center, Penang, Malaysia	141
Table 4.63	Total cholesterol, triglyceride, LDL-cholesterol and HDL-cholesterol (baseline, first followed up, second followed up) Value Based on Duration of Stroke Ischemic Among Hemodialysed Patients in a Hemodialysis Center Penang, Malaysia	142
Table 4.64	Comorbidities or Complications of diabetic and/ hypertensive Patients who undergone Hemodialysis in a Hemodialysis Centre, Jakarta, Indonesia, and Penang, Malaysia	144
Table 4.65	Probability of Dying (Cox-Regression) Based on Potential Complications Among Hypertensive/Diabetic Patients Who Undergone Hemodialysis (Prospective Sample/9 Months Followed up)	145
Table 4.66	Cause of ESRD, Supplement to prevent from loss of Ca, Thyroidectomy, Hyperparathyroidism, Amlodipine Used And Perindopril Used Based on IHD Complication Among Hypertensive/Diabetic Patients Who Undergone Hemodialysis (Prospective Sample/9 Months Followed up) in a HD Center Penang, Malaysia	146



Table 4.67	Frequency of HD Since First HD Based on IHD Complication Among Hemodialysed Patients Who Had Been Followed-up for 9 Months in a HD Center Penang, Malaysia	147
Table 4.68	Duration of IHD from first time on HD and Frequency of HD from first time on HD Among Hemodialysed Patients Who Had Been Followed-up for 9 Months in a Hemodialysis Center Penang, Malaysia	147
Table4.69	Dyslipidemia, Hyperparathyroidism, Smoking-status, Parathyroidectomy, Supplement to prevent from loss of Ca, Amlodipine and Perindopril Used Based on Duration of IHD from first time on HD Among Hemodialysed Patients Who Had Been Followed-up for 9 Months in a HD Center Penang, Malaysia	148
Table 4.70	Total Cholesterol, Triglyceride, LDL-Cholesterol, HDL-Cholesterol, FBS, Hgb, Sodium-post, Potassium pre-post (baseline, first followed up, second followed up) Based on Duration of IHD from first time on HD Among Hemodialysed Patients Who Had Been Followed-up for 9 Months in a Hemodialysis Center Penang, Malaysia	149
Table 4.71	Duration of heart disease from first time on HD Based on Dyslipidemia Complication Among Hemodialysed patients Who Had Been Followed up for 9 Months in a HD center, Jakarta, Indonesia and Penang, Malaysia	151
Table 4.72	Duration of heart disease from first time on HD Based on Duration of hypertensive and Duration of Diabetic Among Hemodialysed patients Who Had Been Followed up for 9 Months in a HD center, Jakarta, Indonesia and Penang, Malaysia	152
Table 4.73	Duration of heart disease from first time on HD and Frequency of HD from first time on HD Among Hemodialysed Patients Who Had Been Followed up for 9 Months in a Hemodialysis Center Jakarta, Indonesia, and Penang, Malaysia	153
Table 4.74	Total Cholesterol, Triglyceride, LDL-Cholesterol, HDL-Cholesterol, FBS, Hgb, Sodium pre-post, Potassium pre-post (baseline, first followed up, second followed up) and Duration of heart disease from first time on HD Among Hemodialysed patients Who Had Been Followed up for 9 Months in a Hemodialysis Center Penang, Malaysia	154
Table 4.75	The Number of Hemodialysed Patients Who Diagnosed Heart Disease Based on CKD Being Diagnosed (year) Among	156

9 Months Followed-up of Hemodialysed Patients in  
a Hemodialysis Center Jakarta, Indonesia and Penang, Malaysia

Table 4.76	Frequency of HD Since First HD Based on Dyslipidemia Drugs Used Among Hemodialysed Patients Who Had Been Followed up for 9 Months in a HD Center Jakarta, Indonesia and Penang, Malaysia	157
Table 4.77	Duration of IHD Since First HD Based on Dyslipidemia Drugs Used Among Hemodialysed patients Who Had Been Followed up for 9 Months in a HD Center Penang, Malaysia	157
Table 4.78	Frequency of HD Since First HD Based on Anemia Complication Among Hemodialysed Patients Who Had Been Followed up for 9 Months in a HD Center Jakarta, Indonesia	158
Table 4.79	Anemia and Mont's Life since First HD Among Hemodialysed Patients Who Had Died Last 5 Years in a HD Center Jakarta, Indonesia	158
Table 4.80	Frequency of HD Since First HD Based on Hepatitis Complication Among Hemodialysed Patients Who Had Been Followed-up for 9 Months in a HD Center Jakarta, Indonesia, and Penang, Malaysia	159
Table 4.81	The number of patients who undergone Hemodialysis with Hepatitis B, Hepatitis C and Both Hepatitis B and C in a HD Center Jakarta, Indonesia and Penang, Malaysia	160
Table 4.82	ALP, ALT (baseline, first followed up, second followed up) Value Based on Duration of Hemodialysis (Year) Among Hemodialysed Patients Who Had Been Followed-up for 9 Months in a Hemodialysis Center Penang, Malaysia	161
Table 4.83	ALP, ALT (baseline, second followed up, third followed up) Based on Liver Infection Among Hemodialysed Patients Who Had Been Followed-up for 9 Months in a Hemodialysis Center Penang, Malaysia	163
Table 4.84	Baseline and Second Followed-up of ALP and ALT Among Hemodialysed Patients Who Had Been Followed-up for 9 Months in a Hemodialysis Center Penang, Malaysia	164

Table 4.85	Baseline, First Followed up and Second Followed up of ALP and ALT Based on Duration of liver infection Among Hemodialysed Patients Who Had Been Followed-up for 9 Months in a Hemodialysis Center Penang, Malaysia	165
Table 4.86	Liver infection and Month's Life since first HD Among Hemodialysed Patients Who Had Died Last 5 Years in a HD Center Jakarta, Indonesia	165
Table 4.87	The Number of Hemodialysed Patients Who Had Liver Infection Based on the Month's Life Since First HD Among Hemodialysed Patients Who Had Died in Last 5 Years in a HD Center, Jakarta, Indonesia	166
Table 4.88	First Followed-up, Second Followed-up and Third Followed-up of SGPT and SGOT for Liver Infection Among Hemodialysed Patients Who Had Died Last 5 Years in a Hemodialysis Center Jakarta, Indonesia	167
Table 4.89	First Followed-up, Second Followed-up and Third Followed-up of SGPT and SGOT Based on Month's Life Since First HD Among Hemodialysed Patients Who Had Died Last 5 years in a Hemodialysis Center Jakarta, Indonesia	168
Table 4.90	First and Third Followed-up of SGPT and SGOT Among Hemodialysed Patients Who Had Died Last 5 years in a Hemodialysis Center Jakarta, Indonesia	170
Table 4.91	Overall Comparisons for Survival Analysis of Diabetic and / or Hypertensive Patients Who Undergone Hemodialysis and Had Been Followed up for 9 Months in a HD Center Jakarta, Indonesia	170
Table 4.92	Overall Comparisons for Survival Analysis of Diabetic and / or Hypertensive Patients Who Undergone Hemodialysis and Had Been Followed up for 9 Months in a HD Center Penang, Malaysia	172
Table 4.93	The Number and the Percentage of HD Patients Who Died From 2010 to 2014 in Cempaka Putih Islamic Hospital, Jakarta, Indonesia	175
Table 4.94	The Number and the Percentage of HD Patients Who Died From 2011 to 2015 in General Hospital Pulau Pinang, Malaysia.	177
Table 4.95	The Number of Hemodialysed Patients	185

## LIST OF FIGURES

	<b>Page</b>	
Figure 2.1	Complications of renal failure (Adopted from Book “Essentials of 30 Pathophysiology; Concepts of Altered Health States” (Porth, 2011))	
Figure 2.2	Hypertension Management Algorithm (JNC 8) Adopted from 32 Journal North American Journal of Medical Sciences (Nicole et al., 2015)	
Figure 2.3	Pathophysiological links between potential contributors to 37 mortality in chronic kidney failure, Adopted from Lancet Journal (Ortiz et al., 2014)	
Figure 3.1	Research Framework of the Study	56
Figure 4.1	Prevalence of Hemodialysed patients by Gender for KDQoL-24 75 Assessment	
Figure 4.2	Prevalence of Hemodialysed patients by Age for KDQoL-24 75 Assessment	
Figure 4.3	Survival Analysis of Diabetic and / or Hypertensive Patients Who 171 Undergone Hemodialysis Based On the Duration/Session of Hemodialysis Among Hemodialysed patients Who Had Been Followed up for 9 Months in a HD Center Jakarta, Indonesia.	
Figure 4.4	Survival Analysis of Diabetic and / or Hypertensive Patients Who 173 Undergone Hemodialysis Based On the Duration/Session of Hemodialysis Among Hemodialysed patients Who Had Been Followed up for 9 Months in a HD Center Penang, Malaysia.	
Figure 4.5	The Number of HD Patients Who Died in last 5 years at HD Unit 174 Cempaka Putih Islamic Hospital, Jakarta, Indonesia	
Figure 4.6	The Number of HD Patients Who Died in Last 5 years at HD unit 176 General Hospital Pulau Pinang, Malaysia	

Figure 4.7 The Number of HD patients during the study at HD ward 178 Cempaka Putih Islamic Hospital, Jakarta, Indonesia

Figure 4.8 The Number of HD patients during the study at HD ward General 179 Hospital, Penang, Malaysia

## LIST OF ABBREVIATION

ALP	Alkaline Phosphatase
ALT	Alanine Amino Transferase
ATP	Adenosine Tri Phosphate
ARF	Acute Renal Failure
AE	Adverse Event
Ca	Calcium
CHF	Congestive Heart Failure
CKD	Chronic Kidney Disease
CRC	Clinical Research Center
CV	Cardiovascular
DM	Diabetic Mellitus
EPO	Erythropoietin
ERBP	European Renal Best Practice
ESRD	End-Stage Renal Disease
FBS	Fasting Blood Sugar
GI	Gastro Intestinal
HB	Hemoglobin
HBV	Hepatitis B Viral
HCV	Hepatitis C Viral
HD	Hemodialysis
HRQOL	Health Related Quality of Life
HTN	Hypertensive
ISDN	Isosorbide Dinitrate
IHD	Ischemic Heart Disease
KDIGO	Kidney Disease Improving Global Outcomes

KDOQI	Kidney Disease Outcomes Quality Initiative
KDQoL	Kidney Disease Quality of Life
N	Number
NKF	National Kidney Foundation
PERNEFRI	Persatuan Nefrologi Republik Indonesia
PSQI	Pittsburg Sleep Quality Index
PTH	Parathyroid Hormone
SBP	Systole Blood Pressure
SD	Standard Deviation
SGOT	Serum Glutamic Oxoloacetic Transaminase
SGPT	Serum Glutamic- Pyruvic Transaminase
SPSS	Statistical Package for Social Sciences
UDD	Unconscious During Dialysis

**DAPATAN TERAPEUTIK DAN MORTALITI YANG BERKAITAN  
DENGAN HEMODIALISIS DALAM KALANGAN PESAKIT HIPERTENSI  
DAN DIABETES DI JAKARTA, INDONESIA DAN PENANG, MALAYSIA**

**ABSTRAK**

Dapatan terapeutik pesakit hemodialysis biasanya bergantung kepada farmakoterapi yang betul yang diberikan dan susulan pesakit. Berdasarkan kejadian kematian yang tinggi dalam kategori ini, satu kajian telah dijalankan di kedua-dua negara, Indonesia dan Malaysia. Sejumlah 455 pesakit dari pusat HD Jakarta dan Pulau Pinang telah dimasukkan ke dalam kajian ini berdasarkan kriteria inklusi dan pengecualian. Penilaian retrospektif sebanyak 199 pesakit di kedua-dua negara turut dimasukkan. Semua pesakit yang memenuhi kriteria telah dimasukkan ke pusat HD Pulau Pinang dan Jakarta sebagai kemudahan sampling. Dalam 256 pesakit hemodialysis yang dinilai, 14.8% mempunyai diabetes mellitus, 55.1% mempunyai hipertensi dan 30.1% mempunyai diabetes mellitus dan hipertensi. Semua data yang dihasilkan pada borang pengumpulan data yang sah dan juga semua pesakit telah diwawancara secara prospektif melalui soal selidik yang telah ditetapkan. Kesemua pesakit akan disusuli selama sembilan bulan di kedua-dua pusat tersebut. Berdasarkan penilaian KDQoL-SF24, perbezaan antara pusat-pusat HD di Jakarta dan Pulau Pinang didapati dalam beban penyakit buah pinggang, status kerja dan sokongan sosial. Walau bagaimanapun, penilaian kesihatan keseluruhan bagi kedua-dua negara adalah lebih daripada markah standard ( $> 59.37 \pm 19.54$ ). Tempoh penyakit kardiovaskular meningkatkan risiko kematian lebih daripada 2 kali di kedua-dua pusat Indonesia dan Malaysia semasa waktu susulan. Di samping itu,



pesakit yang menjalani hemodialisis di Indonesia menunjukkan hubungan yang signifikan ( $P = 0.006$ ) antara tempoh penyakit kardiovaskular dan risiko kematian dengan 23% daripada pesakit ini mempunyai tempoh penyakit kardiovaskular  $\leq 5$  tahun dan hanya 3.4% daripada pesakit ini mempunyai tempoh penyakit kardiovaskular  $\geq 6$  tahun. Hasilnya menunjukkan bahawa tiada ruang berasingan untuk pesakit hemodialysed yang mempunyai hepatitis C di pusat HD Jakarta, Indonesia. Bagaimanapun, di pusat HD di Pulau Pinang, Malaysia, bilik berasingan wujud bagi pesakit yang mempunyai hemodialysed yang mempunyai hepatitis C. Keadaan di atas menerangkan peningkatan hepatitis di kalangan pesakit hemodialis di pusat HD Jakarta, Indonesia (pemeriksaan hepatitis C pertama mencatatkan 46 pesakit hemodialysed hepatitis C manakala tindak lanjut kedua menyaksikan bilangan pesakit meningkat kepada 60). Tambahan pula, 34% pesakit hemodialisis mempunyai hepatitis selepas susulan dan 58,38% pesakit meninggal dengan komplikasi hepatitis. Lebih-lebih lagi, lebih daripada 70% pesakit di Pulau Pinang diberi suplemen untuk menyokong farmakoterapi keadaan hemodialysed manakala beberapa kes telah diperhatikan di Jakarta. Ini mengakibatkan kadar mortaliti (35%) yang lebih tinggi di Jakarta sedangkan di Pulau Pinang kurang daripada 12% kematian didapati. Perbezaan dalam peruntukan sistem farmakoterapi dan penjagaan kesihatan antara kedua-dua negara menyumbang kepada perubahan dalam hasil terapeutik. Oleh itu, pesakit di Pulau Pinang mempunyai kualiti kehidupan yang lebih baik, kadar kelangsungan hidup dan kurang komplikasi berbanding Indonesia.

**THERAPEUTIC OUTCOMES AND MORTALITY RELATED TO  
HEMODIALYSIS AMONG HOSPITALIZED HYPERTENSIVE AND  
DIABETIC PATIENTS IN JAKARTA, INDONESIA AND PENANG,  
MALAYSIA**

**ABSTRACT**

Therapeutic outcomes of hemodialysed patients usually depend on proper pharmacotherapy given and follow up of the patients. Based on the high mortality incidence of this category, a study was conducted in both countries, Indonesia and Malaysia. A total of 455 patients from HD center Jakarta and Penang were included in this study based on inclusion and exclusion criteria. A retrospective evaluation of 199 patients in both countries were also included. All patients that fulfilled the criteria were included in HD center Penang and Jakarta as convenience sampling. In 256 hemodialysed patients who were evaluated by prospective, 14.8 % had diabetes mellitus, 55.1% had hypertension and 30.1 % had diabetes mellitus and hypertension. All the data was produced on a validated data collection form and also all the patients were interviewed prospectively through an already established questionnaire. All the prospective patients were followed up for nine months in both centers. Based on the assessment of KDQoL-SF24, the differences between HD centers in Jakarta and Penang were found in the burden of kidney disease, work status and social support. However, overall health rating for both countries were more than standard score ( $> 59.37 \pm 19.54$ ). Duration of cardiovascular disease elevated risk of death more than 2 times in both centers of Indonesia and Malaysia during the follow up time. In addition, patients who undergone hemodialysis in Indonesia showed significant

relationship ( $P = 0.006$ ) between duration of cardiovascular and probability of dying with 23% of these patients had duration of cardiovascular diseases  $\leq 5$  years and only 3.4 % of these patients had duration of cardiovascular diseases  $\geq 6$  years. The result further indicated that there was no separate room available for hemodialysed patients with hepatitis C in HD center Jakarta, Indonesia. However, at the HD center in Penang, Malaysia, a separate room existed for hemodialysed patients having hepatitis C. The above situation explains the increase of hepatitis among hemodialysed patients in HD center Jakarta, Indonesia (the first hepatitis C check noted 46 hemodialysed patients having hepatitis C while the second follow up saw number of patients increased to 60). Furthermore, 34 % hemodialysed patients had hepatitis upon follow up and 58.38% patients died with hepatitis complication. Moreover, more than 70 % patients in Penang were given supplement to support the pharmacotherapy of the hemodialysed condition while very few cases were noted in Jakarta. This resulted in higher mortality (35%) rate in Jakarta whereas in Penang less than 12 % of mortality were found. The differences in pharmacotherapy and healthcare system provisions between the two countries contributed to the variation in the therapeutic outcomes. Thus, patients in Penang have better quality of life, survival rate and less complication compared to Indonesia.

## CHAPTER 1 INTRODUCTION

### 1.1 Introduction

Hemodialysis is one of the processes in replacing kidney function (Sitprija, 2003). Patients who are doing hemodialysis will be engaged with this treatment for a long time or may be as long as their life (Koda-Kimble, Mary Anne, Young LY, Alldrege, BK, Corelli, RL, Guglielmo, BJ, Kradjan, WA, Williams, 2008). Prevalence and mortality of hemodialysis are found all over the world (Anand, Khanam, & Finkelstein, 2014). Indonesia and Malaysia are not exempted on this (Indonesian Renal Registry, 2014) (Ministry of Health Malaysia, 2012).

Usually patients who requiring hemodialysis are patients with End-Stage Renal Disease (ESRD) and this disease is a worldwide public health problem (Kidney, 2014) and it is the final stage of chronic kidney disease (Dasari, Venkateshwarlu, & Venisetty, 2014). At this stage, the kidneys are no longer able to remove enough wastes and excess fluids from the body (Dasari et al., 2014). There are some risk factors for ESRD such as dietary habit, using of drugs in a long time, loss of body fluid, infection, complication of disease and family history (Koda-Kimble, Mary Anne, Young LY, Alldrege, BK, Corelli, RL, Guglielmo, BJ, Kradjan, WA, Williams, 2008). Taking a good care for this disease will minimize the complication, which can occur among patients on hemodialysis.

The most common risk factors for ESRD are diabetes and hypertension (Indonesian renal Registry, 2012; Ministry of Health Malaysia, 2013). The prevalence of diabetes, metabolic risk factors and other indicators of renal disease provided an increased understanding of the burden of kidney disease within the Australian community, and applicable worldwide (Kidney Health Australia, 2016).

Almost in each country, ESRD prevalence increases every year (Arikan & Tuglular, 2005). ESRD affects over 400,000 patients in North America requiring dialysis (Lacson et.al, 2012). Moreover, it is increasing as many as 25 million people in the United States, and more than 500,000 have end-stage renal disease (Pinho, Silva, & Pierin, 2015; United States Renal Data System, 2015). According to the Karger study, at least 2.9 million people need dialysis in Asia based on modelling data suggestion (Prasad, 2015).

Hemodialysis improves serum creatinine, albumin and prealbumin, normalizes the protein catabolic rate (nPCR) as well as increases the dietary intake of patients (Himmelfarb & Ikizler, 2010). Despite modern technology and medicines, mortality on dialysis continues to be high with an average 5-year survival of approximately 33% and 50% of patients with and without diabetes respectively (Lacson et.al, 2012). There is a high prevalence patients undergoing hemodialysis all over the world is one of the big problems and can be solved while minimizing the risk factors. Furthermore, mortality rate has also increased in undergoing hemodialysis (CDC & Centers for Disease Control and Prevention, 2014; Committee & Akiba, Takashi; Nakai, Shigeru; Shinzato, Toru; Yamazaki, Chikao; Kitaoka, Tateki; Kubo, Kazuo; Maeda, 2000).

Patient condition should be considered prior to hemodialysis because the emergence of other diseases would be very likely such as infection. Infection is common among chronic hemodialysed patients (Miller et al., 2016). Hence, leucocyte level should be checked before hemodialysis commenced especially if patients were prescribed antibiotic due to infection (Miller et al., 2016). In achieving the good clinical outcomes, patients should get good treatment based on the guideline provided by Kidney Disease Outcomes Quality Initiative (KDOQI).

Indonesia and Malaysia are the neighboring countries with similarities such as dietary habit and the high incidence of renal failure (Indonesian renal Registry, 2012; ). Most of the ESRD patients in both countries have diabetic and/ hypertensive as the cause of renal failure (Indonesian Renal Registry, 2012) (Ministry of Health Malaysia, 2013) but the clinical outcomes relate to mortality incidence might be different between both countries.

Malaysia is the closest country to Indonesia where the more attention given to nephrology disease. It is proven by the detail report of National Renal Registry (NRR) and the availability of the complete information from Malaysian Society Nephrology about nephrology field.

Indonesia is one of the countries with high prevalence of hemodialysed patients (Indonesian Renal Registry, 2014). Lack of publication on clinical practice in Indonesia is one of the challenges in this research. Clinical practice is one of the factors that determine mortality rate and clinical outcome of the treatment.

The duration of hemodialysis is closely related to the efficiency and adequacy of hemodialysis, so long hemodialysis is influenced by the rate of progression of uremia due to worsening of renal function and comorbidity factors, as well as the speed of blood flow and dialysate flow rate (National Kidney Foundation, 2002).

There are 3 groups of hemodialysis duration per session in Indonesia; < 3 hours, 3-4 hours and > 4 hours per session. In this report, it was discovered that hemodialysis duration for category 3-4 hours per session had the biggest number in hemodialysed patients also for 2 times frequency of hemodialysis per week, it should be more than 5 hours per session in term of hemodialysis duration (Indonesian Renal Registry, 2014).

In Malaysia, there are 6 groups of hemodialysis duration per session;  $\leq 3$  hours, 3.5 hours, 4 hours, 4.5 hours, 5 hours and  $> 5$  hours. In 2012, almost 98.1% (25,247 of 25,739 patients) of Malaysian hemodialysed patients had hemodialysis 3 times per week however 98.8% (25,429 of 25,742 patients) did hemodialysis 4 hours per session (National Renal Registry Malaysia, 2013).

According to the Association of nephrologist in Indonesia (Pernefri) recommendation, isolation and using special hemodialysis machine are not necessary for hemodialysed patients who has been infected by hepatitis C viral (Recommendation for controlling hepatitis B and hepatitis C viral infection by Pernefri) while Ministry of Health Malaysia recommends that hemodialysed patients who has been infected by hepatitis C viral will be dialyzed in a separate room or a separate area with a fixed partition and dedicated machines.

Furthermore, a study conducted in Indonesia showed 15353 (0.006%) new patients undergone hemodialysis in 2011 and increased to 19621 (0.008%) patients in 2012 (Indonesian renal Registry, 2012). In Malaysia, indicated 5930 (0.020%) new hemodialysed patients in 2011 but it was decreased slightly at 5830 (0.019%) patients in 2012 (National Renal Registry Malaysia, 2013). Indonesia increased at 33.3% while Malaysia descended at 5 % in the same time at 2012 (Indonesian renal Registry, 2012; Ministry of Health Malaysia, 2013).

### **1.1 Prevalence of Mortality of Hemodialysed patients in the World**

According to the World Health Organization (2005) approximately 35 million people died due to chronic kidney disease (Levey et al., 2007). The prevalence of ESRD in the world were more than 2 million people (Ortiz *et.al.*, 2014). Unadjusted 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). Infection was the primary cause of death among hemodialysed patients and it was followed by cardiovascular as a secondary cause for mortality among these patients (Ortiz et al., 2014).

### **1.3 Prevalence of Mortality of Hemodialysed patients in Indonesia**

Indonesian Renal Registry (IRR, 2012) described that mortality cause due to cardiovascular and cerebrovascular were 1557 patients and 395 patients among 3332 hemodialysed patients respectively (Indonesian Renal Registry, 2012). The largest causes of death was cardiovascular (1090 patients) and **it was followed** by cerebrovascular (233 patients) among 2221 all hemodialysed patients (Indonesian Renal Registry, 2014).

In 2014, one-month survival of all hemodialysed patients in Indonesia was 87.3% while one-year survival was 46.7% in 2014 (Indonesian Renal Registry, 2014). The reason and the percentage of patients who discontinued hemodialysis in 2014 are 49% died, 25% for unknown reason, 23% dropped out and only 1% changed the hemodialysis method to peritoneal dialysis or to the renal transplantation (Indonesian Renal Registry, 2014).



#### **1.4 Prevalence of Mortality of Hemodialysed patients in Malaysia**

The Malaysian dialysis & transplant 20<sup>th</sup> reported that 3017 hemodialysed patients died in 2012 while some of them were caused by cardiovascular (977 patients) and 441 patients died at home (National Renal Registry Malaysia, 2013). The death rate increased in 2013 with 3437 patients, some of the death were caused by cardiovascular (1213 patients) (National Renal Registry Malaysia, 2013).

In 2012, in 6966 patients who were on dialysis have shown survival in 6010 patients by the end of one-year survival function. Furthermore, in 2013, almost 6683 patients showed better survival of 87% in patients registered from 2011 (National Renal Registry Malaysia, 2013).

#### **1.2 Therapeutic Outcomes of Hemodialysed patients**

Usually, hemodialysed patients have hypertensive, diabetic, anemia, mineral & bone disorder and Cardiovascular Disease (CV). As mentioned in the background, diabetic and/ hypertensive are the most cause of the ESRD. For hypertensive, aggressive blood pressure control is one way to delay the decline in renal function in patients with Chronic Kidney Disease (CKD) (Aram V. Chobanian, George L. Bakris, Henry R. Black, William C. Cushman, Lee A. Green, Joseph L. Izzo, 2004).

Antihypertensive therapy prevents kidney damage and slow the rate of progression of CKD in both diabetic and No-diabetic Patients (Kidney Disease Outcomes Quality Initiative, 2004). For diabetic, the majority of drugs available to treat hyperglycemia, and especially first-generation sulfonylureas and  $\alpha$ -glucosidase inhibitors, are affected by kidney function and therefore should be either be avoided or used in reduced doses by patients with CKD (Cavanaugh, 2007).

Anemia, mineral & bone disorder and cardiovascular disease are complications of ESRD (Marry Anne & Alledredge, 2013). Anemia may develop early during the course of CKD due to inadequate synthesis of erythropoietin by the kidneys (Arora, 2016). Both iron supplementation and injectable erythropoiesis-stimulating agents (ESAs) have been used to correct anemia (Besarab & W.Coyne, 2010). With erythropoietin treatment, the goal is a hemoglobin level of 10-12 g/dL, as normalization of hemoglobin in patients with CKD stages 4-5 has been associated with an increased risk of adverse outcomes **when patients use EPO in high dose** (Arora, 2016).

Treatment of abnormal mineral homeostasis in patients with CKD includes the following (National Kidney Foundation, 2009) are lowering high serum phosphorus levels, maintaining serum calcium levels and lowering serum parathyroid hormone levels.

Patients with CKD are at high risk for developing CVD complication; the risk increases as estimated glomerular filtration rate (eGFR) declines. CVD is the leading cause of mortality in CKD (National Kidney Disease Education Program, 2015). Adults aged 50 years or above with an estimated glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m<sup>2</sup> who are not being treated with in long-term dialysis or kidney transplantation are treated with a statin or a statin plus ezetimibe (Barclay, 2013).

Adults aged 18-49 years with an estimated GFR of less than 60 mL/min/1.73m<sup>2</sup> who are not being treated with dialysis or kidney transplantation are treated with statins if they have coronary disease, diabetes, prior ischemic stroke, or an estimated 10-year incidence of coronary death or no fatal-myocardial infarction exceeding 10% (Barclay, 2013).

### **1.3 Research Question**

The background of this study has explained the big issue in term of hemodialysis not only the prevalence but followed by the rising mortality among those patients. The mortality incidence can be controlled by the good therapeutic outcome. Few publication about the comparison study on hemodialysis especially between two Asian countries has created some questions which needs to be answered;

- 1) The comparison of therapeutic results and expected clinical outcomes achieved among diabetic and/or hypertensive patients who undergo hemodialysis in both countries.
- 2) Evaluation of the rate of mortality among hypertensive and diabetic patients who undergo hemodialysis in Indonesia and Malaysia.

### **1.4 Rationale of the study**

ESRD is burdensome on public health. Prevalence and mortality associated with ESRD depends on the treatment and clinical practice. Each hospital has difference clinical pattern on treatment, hence gives impact to quality of life and clinical outcome. Causal factors of ESRD could be sources of severe of disease although complications that occur during hemodialysis treatment might be the main thing of it. Before that, the good pharmacotherapy given must be the priority to achieve the good clinical outcome.

Kidney Disease Outcomes Quality Initiative (KDOQI) is one of the worldwide guideline for kidney disease patients although each country has their own guideline still refers to KDOQI guideline. Having the guideline provide assumption that the treatment should be going well but some facts tell opposite due to

unexpected factors. Better treatment or improve treatment outcome only can be done by evaluating the clinical practice from comparative between two hemodialysis centers. Jakarta and Penang are big cities that also have big hemodialysis center which is expected to help in evaluating the predictors of mortality that can affects better treatment outcomes.

### **1.5 Significant of the study**

This is the first study which compared therapeutic outcome and mortality between two Asian countries (Indonesia and Malaysia) done in two HD centers (Jakarta, Penang). This research involves two types of data/samples (retrospective and prospective). Retrospective samples were done by taking data of hemodialysed patients who had died last five years and prospective samples were collected by following and evaluating hemodialysed patients for 9 months in both countries.

This research may help in evaluating of clinical practice, treatment outcomes and predictors of mortality. Previous studies in Malaysia reported mortality factors among hemodialysis covering only few factors such as coronary heart disease, peripheral vascular disease, acute myocardial infarction and congestive heart failure (N. B. Yusop, Mun, Shariff, & Huat, 2013). National Renal Research (NRR) report of all of kidney disease treatment outcome in Malaysia does not give the detail on all incidence going on and such as improving or decreasing of mortality incidence, the relationship between practice pattern and clinical outcome and others causal factors which correlate with mortality but Malaysia has their own guideline in term of hemodialysis and research about hemodialysis are conducted regularly. However, with Indonesia, general information is provided about hemodialysis by the Indonesia Renal Registry report but there is lack of published article related to hemodialysis among hemodialysed patients in Indonesia.

In this research, the first objective, quality of life patients for a hemodialysis center in Penang, the evaluation was carried out by using Kidney Disease Quality of Life (KDQOL)-24 questionnaire which was adopted from KDQOL-24 Malaysian version while for a hemodialysis center in Jakarta, KDQOL-24 questionnaire translated to Indonesian language was used for pilot study to assess the validity of the questionnaire.

The other objectives such as clinical pattern, causal factors, complications, clinical outcome and mortality rate of hemodialysed patients for both hemodialysis center were collecting by assessing retrospective and prospective data.

## **1.6 Objectives**

Due to the novelty comparative study about therapeutic outcome and mortality among hemodialysed patients between two Asian countries, general objective was about evaluation related to these issues in both countries. As mentioned on the research questions, therapeutic outcomes and mortality rate among hypertensive and diabetic patients was evaluated for providing answer to clinical outcome achieved in these both countries.

### **1.6.1 General Objective**

Evaluation of the clinical outcomes and mortality rate among hypertensive and diabetic patients on hemodialysis between Indonesia and Malaysia.

### **1.6.2 Specific Objectives**

Specific objectives of this study were created based on the elaboration of the general objective. Demographic data was the first thing that was explored because the study was conducted in two Asian countries. Besides that, few things like clinical

pattern, quality of life patients, potential risk factors, differences of the pharmacotherapy, potential complications and mortality rate was included as the specific objectives which has been conducted to answer the clinical outcome achieved in these two Asian countries. The specific objectives answered on this study are;

- 1) Evaluation of demographic data of patients and practice pattern that correlate with the clinical outcome among hypertensive and diabetic patients on hemodialysis for Indonesia and Malaysia.
- 2) Assessment of the health-related quality of life (HRQOL) patients using KDQOL (Kidney Disease Quality of Life)-24 tool.
- 3) Evaluation of the potential risk factors of ESRD that correlate with the clinical outcome among hypertensive and diabetic patients on hemodialysis between Indonesia and Malaysia.
- 4) Evaluation of the differences of pharmacotherapy among ESRD patients who undergone hemodialysis between Indonesia and Malaysia.
- 5) Evaluation of the potential complications that occur among ESRD patients who undergo hemodialysis and the mortality rate in both countries.

## CHAPTER 2 LITERATURE REVIEW

### 2.1 Hemodialysis

End-stage renal disease can be treated by renal replacement therapies, such as Hemodialysis (HD), Transplantation, and Peritoneal Dialysis (PD) (Indian Society of Nephrology, 2014). HD increases expected lifetime of the patients minimizing the effects of neurological complications (Denhaerynck, 2007; Goksan, Kaarali-Savrun, Ertan, & Saurun, 2004) and improves serum creatinine, albumin and prealbumin, normalises the protein catabolic rate (nPCR) as well as increases the dietary intake of patients (N. B. M. Yusop, Mun, Shariff, & Huat, 2013). Despite its advantages, HD is highly associated with malnutrition and lower quality of life (QOL) (T. Chang, Nam, Shin, & Kang, 2015). Severe malnutrition among HD patients in Malaysia was reported to be approximately 4.6% - 19%, while 72% - 90.9% are mildly malnourished (N. B. M. Yusop et al., 2013). Hemodialysis dose given is generally 2 times a week with each hemodialysis for 5 hours or as many as three times a week with each hemodialysis for 4 hours (Goksan et al., 2004).

### 2.2 Background progression of CKD to ESRD

Chronic Kidney Disease (CKD) is defined as kidney damage or Glomerular Filtration Rate (GFR)  $< 60 \text{ ml/min/1.73 m}^2$  for 3 months or more, irrespective of cause (Draws, P; Rahman, 2009; Levey, et.al, 2005). Evidence of kidney damage, including persistent albuminuria—defined as  $> 30 \text{ mg}$  of urine albumin per gram of urine creatinine (Grimshaw & Eccles, 1998). To understand the background of CKD

to ESRD, identification of CKD progression, risk factors, symptoms and signs of CKD was discussed.

### **2.1.1 Identification of CKD Progression**

CKD can be classified into two (2) categories; GFR and albumin category. For GFR category calculation, filtration rate of the wastes of metabolism in glomerular need to be calculated while albumin value can be seen directly from the result of laboratory value of the patients.

#### **2.2.1.1 GFR Category**

GFR category consist of five (5) stages. There are 1 to 5 where stage 3 can be divided into stage 3A and 3B. For patients who have GFR category in stage 5, kidney failure is showed with GFR less than 15 ml/min/1.73 m<sup>2</sup>. They are referred to End-Stage Renal Disease (ESRD) patients. Progression of chronic kidney disease is in the last stage and the stage kidney does not function anymore. Classification of CKD can be seen in Table 2.1 below;



**Table 2.1 Classification of Chronic Kidney Disease by GFR Category\***

<b>Stage</b>	<b>Description</b>	<b>GFR (ml/min/1,73 m<sup>2</sup>)</b>	<b>Related Terms</b>
1	Kidney Damage with normal or increasing of GFR	≥ 90	Albuminuria, Proteinuria, Hematuria
2	Kidney damage with mild reducing of GFR	60-89	Albuminuria, Proteinuria, Hematuria
3 A	Mildly to moderately decrease	40-59	Chronic Renal Insufficiency,
3B	Moderately to severely decreased	30-44	Early Renal Insufficiency
4	Severe reducing of GFR	15-29	Chronic Renal Insufficiency, Late Renal Insufficiency, Pre- ESRD
5	Kidney Failure	< 15 (or dialysis)	Renal failure, Uremia, End- Stage Renal Disease

**\*Adopted from Journal Annals of Internal Medicine, Kidney International, Faculty Group Practice University of Michigan Health System (UMHS) (Draws, P; Rahman, 2009; Levey, A.S., et.al, 2005; Lukela & et.al, 2014)**

### 2.2.1.2 Albumin Category

Albumin category consist of three (3) stages. There are stage A1, A2 and A3. Stage A3 shows the severe of kidney condition but for stage A1 shows mild of kidney condition. This can be seen in Table 2.2 below:

**Table 2.2 Classification of Chronic Kidney Disease by Albumin Category\***

<b>Stage</b>	<b>Description</b>	<b>Albumin</b>
A1	Normal to mildly increased	< 30 mg/g < 3 mg/mmol
A2	Moderately increased	30-300 mg/g 3- 30 mg/mmol
A3	Severely increased	> 300 mg/g > 30 mg/mmol

**\*Adopted from National Kidney Foundation (NKF, 2013)**

### 2.2.2 Risk Factors of CKD

Risk factors 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 in other 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 (4) categories of risk factors. They are susceptibility, initiation, progression and end-stage factors. Susceptibility factors depend on sociodemographic variables such as age, family history and race. An 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.et.al, 2005). This can be seen in Table 2.3 below;

**Table 2.3 Risk Factors for CKD\***

<b>No</b>	<b>Component</b>	<b>Causal</b>
1	Susceptibility Factors	<ul style="list-style-type: none"> <li>✓ Older Age</li> <li>✓ Family History of CKD</li> <li>✓ Reduction in Kidney Mass</li> <li>✓ Low Birth Weight</li> <li>✓ Racial or Ethnic Minority Status</li> <li>✓ Low Income/ Low EduCation</li> </ul>
2	Initiation Factors	<ul style="list-style-type: none"> <li>✓ Diabetes</li> <li>✓ High Blood Pressure</li> <li>✓ Autoimmune Diseases</li> <li>✓ Systemic Infections</li> <li>✓ Urinary Tract Infections</li> <li>✓ Urinary Stones</li> <li>✓ Lower Urinary Tract Obstruction</li> <li>✓ Drug Toxicity</li> <li>✓ Heredity Disease</li> </ul>
3	Progression Factors	<ul style="list-style-type: none"> <li>✓ Higher Level of Proteinuria</li> <li>✓ Higher Blood Pressure Level</li> <li>✓ Poor Glycemic Control in Diabetes</li> <li>✓ Possibly Dislipidemia</li> <li>✓ Smoking</li> </ul>
4	End-Stage Factors	<ul style="list-style-type: none"> <li>✓ Lower Dialysis Dose</li> <li>✓ Temporary Vascular Access</li> <li>✓ Anemia</li> <li>✓ Low Serum Albumin</li> <li>✓ High Serum Phosphorus</li> <li>✓ Late Referral to the hospital</li> </ul>

**\*Adopted from Journal Kidney International and National Kidney Foundation (Levey, et.al, 2005; NKF, 2002)**

### **2.2.3 CKD Signs and Symptoms**

There are two stages of CKD; early and late stages of CKD. To avoid the severe of the disease, it is important to be aware of the early stages of CKD signs and symptoms. Nausea, edema, pale skin and foamy or bubbly urine are the examples of

early stages of CKD. Elevated blood pressure, stomatitis and anemia are examples of the late stages of CKD. This can be seen in Table 2.4 below;

**Table 2.4 Symptoms and Signs of CKD\***

No	Component	Causal
1	Symptoms and Signs of Early Stages of CKD	<ul style="list-style-type: none"> <li>✓ Weakness</li> <li>✓ Decreased appetite</li> <li>✓ Nausea</li> <li>✓ Changes in urination (polyuria, frequency)</li> <li>✓ Blood in urine or dark-colored urine</li> <li>✓ Foamy or bubbly urine</li> <li>✓ Loin pain</li> <li>✓ Edema</li> <li>✓ Elevated blood pressure</li> <li>✓ Pale skin</li> </ul>
2	Symptoms and Signs of Late (Uremic) Stages of CKD	<ul style="list-style-type: none"> <li>✓ <b>General</b> (<i>lassitude , fatigue , elevated blood pressure , signs of volume overload , decreased mental acuity , intractable hiccups , uremic fetor</i> )</li> <li>✓ <b>Pulmonary</b> (<i>dyspnea , pleural effusion , pulmonary edema , uremic lung</i> )</li> <li>✓ <b>Cardiovascular</b> (<i>periCardial friction rub ,congestive heart failure</i> )</li> <li>✓ <b>Gastrointestinal</b> (<i> anorexia , nausea , vomiting, weight loss , stomatitis , unpleasant taste in the mouth</i> )</li> <li>✓ <b>Neuromuscular</b> (<i> muscular twitches , peripheral sensory and motor neuropathies, muscle cramps , restless legs ,sleep disorders , hyperrefl exia , seizures , encephalopathy , coma</i> )</li> <li>✓ <b>Endocrine-metabolic</b> (<i> decreased libido , amenorrhea , impotence</i> )</li> <li>✓ <b>Hematologic</b> (<i> anemia , bleeding diathesis</i> )</li> </ul>

\*Adopted from book “Management of Chronic Kidney Disease” Springer (Choi, 2012)

## **2.2.4 Comorbidities of CKD**

Hypertension (prevalence 74.5 million in the world) and diabetes (prevalence 23.6 million in the world) are the two most important CKD risk (Abboud & Henrich, 2010; Clinical Practice Recommendations for Primary Care Physicians and Healthcare Providers, 2011) when advanced, it causes a higher risk of mortality (Abboud & Henrich, 2010).

Overall, diabetic prevalence population in the world among ESRD (44%) and HTN (28%) (Clinical Practice Recommendations for Primary Care Physicians and Healthcare Providers, 2011). Together, these two disorders constitute 72% of the causes of ESRD (Clinical Practice Recommendations for Primary Care Physicians and Healthcare Providers, 2011).

### **2.2.4.1 Diabetes Mellitus**

Diabetes is the commonest cause of ESRD requiring renal replacement therapy (Brancati FL, Whelton PK, Randall BL, Neaton JD, Stamier J, 1997; SIGN, 2008). From all-cause ESRD in USA, men with diabetes are more than 12 times greater per year than in men without diabetes (199.0 vs 13.7 cases per 100,000 person years; relative risk (RR) 12.7; 95% confidence interval (CI), 0.5 to 15.4) (BranCati FL, Whelton PK, Randall BL, Neaton JD, Stamier J, 1997; SIGN, 2008). This increased incidence was attributable to both diabetic and non-diabetic nephropathy. In 2005, 0.5% of the population with diabetes who were recorded in the National Diabetes Survey were reported had ESRD complication (Brancati FL, Whelton PK, Randall BL, Neaton JD, Stamier J, 1997; SIGN, 2008).

The connection between kidney and insulin metabolism was well known for many years (Biesenbach & Pohanka, 2011; Horton, Johnson, & Lebovitz, 1968). For insulin excretion the kidneys are one of its target organs (Iglesias & Díez, 2008). Chronic renal failure was associated to multiple alterations in the carbohydrate and insulin metabolism that should be taken into account when treating diabetic patients with altered renal function (Biesenbach & Pohanka, 2011; Defronzo, Andres, Edgar, & Walker, 1973). Effects of kidney dysfunction in dialysis patients who have diabetes are hypoglycemia and hyperglycemia (Rhee et al., 2015). Monitoring of glycemic control among dialysis patients is important to avoid those effects.

Specific therapeutic needs (oral agents or insulin) will be determined based on the degree of insulin resistance or insulin deficiency of patients with renal insufficiency (Biesenbach & Pohanka, 2011; Rabkin, Ryann, & Duckwords, 1984). A good metabolic control is not only important in the early phase of diabetic nephropathy but also in diabetic patients with ESRD (Biesenbach & Pohanka, 2011). It was shown in several studies, that metabolic control under antidiabetic therapy is a predictor for prognosis of patients with renal replacement therapy (Biesenbach & Pohanka, 2011; Morioko, Etmoto, T, & et.al, 2001). A good glycemic control can reduce the progression of atherosclerosis (Biesenbach & Pohanka, 2011; Oomichi, Etmoto, Tabata, & et.al, 2006) and improve the survival in patients treated with hemodialysis (Biesenbach & Pohanka, 2011; C. Kovesdy, Sharma, & Kalandar, 2008). Though, in another study it was suggested that aggressive glycemic control cannot be routinely recommended for all diabetic hemodialysed patients on the basis of reducing mortality risk (Biesenbach & Pohanka, 2011; William, 2007).

The majority of uremic type 2-diabetic patients need insulin, however, a smaller part of these diabetic patients can also be treated with oral antidiabetic agents

(Biesenbach & Pohanka, 2011). Some studies suggest avoiding long-acting insulin, whereas others support its use (Cavanaugh, 2007; Synder & Berns, 2004). One small study comparing type 1 diabetic patients with and without Diabetic Kidney Disease (DKD) demonstrated that clearance was reduced for both regular insulin and insulin lispro; however, the effect of regular insulin was also impaired in patients with DKD (Cavanaugh, 2007; Rave, Heise, Pfutzner, Heinemann, & Sawicki, 2001).

Thus, a higher dose of regular insulin may be required, despite lower clearance in patients with kidney disease. Insulin lispro did not demonstrate any differences in metabolic effects on glucose in patients with or without Diabetic Kidney Disease (DKD) (Cavanaugh, 2007; Rave et al., 2001). Regardless of the form of insulin chosen to treat diabetes, caution must be exercised when administering therapy to patients with kidney disease and frequent blood glucose monitoring may be used to adjust dosing and prevent hypoglycemia (Cavanaugh, 2007)

In 2001, more than 91 million prescriptions were written for oral hyperglycemic agents, and ~ 33% were for sulfonylureas (Cavanaugh, 2007; Wysowski, Armstrong, & Governale, 2003). The clearance of both sulfonylureas and its metabolites was highly dependent on kidney function, and severe prolonged episodes of hypoglycemia as a result of sulfonylurea use have been described in dialysis patients (Cavanaugh, 2007; Krepinsky, Ingram, & Clase, 2000). In patients with stages 3–5 CKD, first-generation sulfonylureas should be avoided. Of the second-generation sulfonylureas, glipizide was recommended because its metabolites are not active, and there was a lower potential for development of hypoglycemia (Gennari, Hood, Greene, Wang, & Levey, 2006).

Metformin is in the *biguanides* class of oral hyperglycemic drugs, which does not exhibit the high risk of hypoglycemia associated with other drug classes used to

treat diabetes (Cavanaugh, 2007). However, special care must be taken when it is used in patients with CKD. There was a risk of development of lactic acidosis, even in patients with mild impairment of kidney function, again likely resulting from the accumulation of the drug and its metabolites (Cavanaugh, 2007; Davidson & Peters, 1997). Metformin was contraindicated in male patients with a serum creatinine > 1.5 mg/dl and in female patients with serum creatinine > 1.4 mg/dl (Cavanaugh, 2007; Gennari et al., 2006).

Metformin was contraindicated with even mild to moderate kidney disease, whereas TZDs did not require dose adjustments for kidney disease and may have an independent beneficial impact on the progression of DKD (Cavanaugh, 2007). A summary of available drug therapies for diabetes and dosing recommendations was presented in Table 2.5.

**Table 2.5 Drug Therapies and Dosing Recommendations for Dialysis Patients\***

No	Administrative of Drugs Given	Drug Therapies and Dosing Recommendations	Notice
1	Intra Peritoneal (IP) or Sub Cutaneous (SC	<b>Insulin</b> = dose reduction of 50 % when GFR is < 10 ml/min/1.73 <sup>1,2,3</sup>	-
2	Oral	<b>Sulfonilureas,</b> Short acting glipizide <sup>2,4</sup>	Acetohexamide, Chlorpropamide, Tolazamide, Tolbutamide should not be used by dialysis patients due to of



			hypoglycemia effect
3	Oral	<b>Meglitinides,</b> Repaglinide <sup>2,4</sup>	Nateglinide is not advised due to hypoglycemia effect
4	Oral	<b>Biguanides</b>	Metformin is 90 % is renally excreted and it should not be used in dialysis patients <sup>5</sup>
5	Oral	<b>Thiazolidinediones (TZD)</b> Pioglitazone reduced risk of Cardiovascular disease morbidity and mortality	Overall this group is promote edema and congestive heart failure For example; Rosiglitazone have shown an increased risk of cardiovascular disease events
6	Oral	<b>Dipeptidyl Peptidase-4 Inhibitors (DPP-4 Inhibitors)</b> Sitagliptin 25 mg/day Saxagliptin 2.5 mg/day after dialysis	Exenatide is not recommended in dialysis patients
7	Oral	<b>Alpha Glucosidase Inhibitors</b>	Acarbose and Miglitol are not advised in

			dialysis patients
8	Oral	<b>Sodium Glucose Cotransporter (SGLT2) Inhibitors</b>	Contraindicated in dialysis patients due to modestly lower elevated blood glucose

\*Summarised from (Rhee et al., 2015); <sup>1</sup> (Kalantar-Zadeh, Derose, Nicholas, Sharma, & Kovesdy, 2009), <sup>2</sup> (Reilly & Berns, 2010), <sup>3</sup> (Charpentier, Riveline, & Varroud-Vial, 2000), <sup>4</sup> (Flynn & Bakris, 2013), <sup>5</sup> (KDIGO, 2012a)

#### 2.2.4.2 Hypertension / High Blood Pressure

Hypertension (HTN) in CKD is considered by default as “resistant HTN”, *ie*, treatment requires 3 or more antihypertensive agents at maximally tolerated doses and one of which must be a diuretic (Indian Society of Nephrology, 2014). The typical Blood Pressure (BP) profile is a Systole Blood Pressure (SBP) greatly exceeding Diastole Blood Pressure (DBP), manifested as an elevated pulse pressure (>55 mmHg) (Indian Society of Nephrology, 2014). Either the SBP or pulse pressure may be increased in hypervolemic/edematous individuals who must often be treated with diuretics (Indian Society of Nephrology, 2014). Many studies have shown that hypertension is a risk factor for CKD (Biesenbach & Pohanka, 2011; Chadban et al., 2003; Coresh, Astor, Greene, Eknoyan, & Levey, 2003; R. Foley et al., 2005; Fox et al., 2004; SIGN, 2008b).

Management hypertension is recently referred to Eight Joint National Committee (JNC8) while blood pressure for patients with all ages CKD present with or without diabetes less than 140/90 mmHg (Nicole, Contino, Jain, Grand, & Hagens, 2015) while JNC 8 is the new guideline for hypertensive which all the physicians should follow. Initiate Angiotensin Converting Enzyme inhibitor (ACEi)

or Angiotensin Receptor Blocker (ARB), alone or combination with other drug class of hypertension is the hypertension treatment which should give to all the CKD patients.

### **2.3 Baseline Assessments for Hemodialysis**

In order to conduct the baseline assessment for age, gender, height, weight, comorbidities (diabetes, peripheral vascular disease, coronary artery disease, congestive heart failure, cerebrovascular disease, cancer), and receipt of pre dialysis care (at least 4 months) must be recorded for each patients to obtain the baseline laboratory values (Williams, Quinn, Callery, Kiss, & Oliver, 2011). Baseline laboratory values (hemoglobin, serum creatinine, urea, albumin, calcium, phosphate, and urea reduction ratio) were the mean values of the first 3 months of dialysis measured during routine monthly blood work and this must be recorded for all HD and PD patients (Williams et al., 2011).

Estimated glomerular filtration rate was also calculated from the last available serum creatinine prior to the start of dialysis (Williams et al., 2011). Access in use was recorded at the start of outpatient dialysis treatment (Williams et al., 2011). Dialysis modality was assigned as either PD or HD at the start of outpatient dialysis and for a secondary analysis after 90 days of dialysis therapy (Williams et al., 2011).