MEDICATION ADHERENCE AMONG CHRONIC KIDNEY DISEASE PATIENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HOSPITAL USM)

NURAINNI BINTI ABDUL MALEK

SCHOOL OF HEALTH SCIENCES

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by

NURAINNI BINTI ABDUL MALEK

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LIST OF ABBREVIATIONS

ACR	- Albumin: Creatinine Ratio
BUN	- Blood Urea Nitrogen
CKD	- Chronic Kidney Disease
DM	- Diabetes Mellitus
ESKD	- End Stage Kidney Disease
GFR	- Glomerular Filtration Rate
HPT	- Hypertension
MMAQ	- Morisky Medication Adherence Questionnaire
WHO	- World Health Organization

KOMPLIANS TERHADAP PENGAMBILAN UBATAN DALAM KALANGAN PESAKIT PENYAKIT BUAH PINGGANG DI HOSPITAL UNIVERSITI SAINS MALAYSIA (HOSPITAL USM)

ABSTRAK

Komplians terhadap pengambilan ubatan didefinisikan sebagai “sejauh mana tingkah laku seseorang sesuai dengan saranan ahli profesional kesihatan yang dipersetujui dalam hal pengambilan ubat-ubatan, mengikuti diet yang dianjurkan dan/atau melaksanakan perubahan gaya hidup". Oleh kerana komplians terhadap pengambilan ubatan adalah penting untuk memperlambatkan proses perkembangan penyakit dan mencegah komplikasi terutama di kalangan pesakit Penyakit Buah Pinggang, Kajian keratan rentas dilakukan untuk menilai tahap komplians terhadap ubatan dalam kalangan pesakit Penyakit Buah Pinggang di Hospital USM. Soal selidik yang digunakan dalam kajian ini adalah soal selidik yang dikendalikan sendiri. Seramai 75 orang pesakit Penyakit Buah Pinggang dari Klink Pakar Perubatan (KPP) dan Chronic Kidney Disease (CKD) Resource Centre di Hospital USM yang memenuhi kriteria inklusi terlibat di dalam kajian ini. Mereka dipilih menggunakan kaedah persampelan rawak kebarangkalian sederhana. Data yang dikumpulkan dianalisis secara statistik menggunakan perisian Statistical Package Social Science (SPSS) versi 25. Kajian ini menunjukkan bahawa 44.0% pesakit Penyakit Buah Pinggang di Hospital USM mempunyai tahap komplians terhadap pengambilan ubatan yang rendah. Selain itu, hasil kajian menunjukkan bahawa 85.3% responden mempunyai tahap kepuasan yang baik terhadap maklumat ubatan yang diberikan oleh pegawai perubatan dan staf farmasi. Sementara itu, 74.7% responden mempunyai tahap kepuasan yang baik dengan Jururawat. Etnik mempunyai perkaitan yang signifikan dengan komplians terhadap pengambilan ubatan ($p = 0.032$). Lupa terhadap pengambilan ubatan, sibuk dan terlepas

temu janji adalah penyebab utama mengapa responden tidak komplian terhadap pengambilan ubatan dalam kalangan responden dalam kajian ini. Kesimpulannya, pengurusan dan strategi yang sesuai harus dibentuk dan ditambahbaik untuk meningkatkan komplians terhadap pengambilan ubatan dalam kalangan pesakit Penyakit Buah Pinggang.

MEDICATION ADHERENCE AMONG CHRONIC KIDNEY DISEASE PATIENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HOSPITAL USM)

ABSTRACT

Medication adherence is defined as "the extent to which a person's behaviour corresponds with the agreed recommendations of a healthcare provider in terms of taking medicines, following the recommended diet and/or executing lifestyle changes". As medication adherence is important to slow the disease progression and prevent complication especially among Chronic Kidney Disease (CKD) patients, a cross-sectional study was carried out to assess the medication adherence among CKD patients in Hospital USM. Data was collected using a self-administered questionnaire. A total of 75 CKD patients from *Klinik Pakar Perubatan* (KPP) and Chronic Kidney Disease (CKD) Resource Centre in Hospital USM, who fulfilled the inclusion criteria were involved in this study. They were selected through probability simple random sampling method. Data collected were statistically analysed using the Statistical Package Social Science (SPSS) software version of 25. This study shows that 44.0% of the CKD patients in Hospital USM had low medication adherence. Moreover, the results showed that 85.3% of respondents had a good satisfaction level on medication information provided by both medical officer and pharmacists. While 74.7% of the respondents had a good satisfaction level with information from the nurses. Ethnicity was found to be significantly associated to non-adherence to medication ($p = 0.032$). Forgetfulness, busy and missed appointments were found to be the most common reasons for non-adherence among CKD patients in Hospital USM. In conclusion, suitable management and strategies should be developed and improve to minimise barriers to medication adherence among CKD patients.

CHAPTER 1 INTRODUCTION

1.1 Background to the Study

This chapter introduces Chronic Kidney Disease (CKD), medication adherence and factors associated with non-adherence to medication among Chronic Kidney Disease.

1.1.1 Chronic Kidney Disease

Chronic kidney disease (CKD) can be defined as kidney damage or a condition when the function of kidney reduces with a glomerular filtration rate (GFR) of less than 60 millilitres/minutes (ml/min) per 1.73 square meter (m2), or a kidney damage marker of at least three months, irrespective of the underlying cause (Jain et al., 2018; Verma et al., 2018; Webster et al., 2017). There are a few markers of kidney damage include albuminuria (albumin: creatinine ratio [ACR] ≥30mg/g), urinary sediment abnormality, electrolyte or other abnormality due to tubular disorder, abnormalities on histology, structural abnormalities detected by imaging and lastly history of kidney transplantation (Webster et al., 2017).

Chronic Kidney Disease (CKD) can be classified based on glomerular filtration rate (GFR) (classified as G1 – G5) and Albumin: Creatinine Ratio (ACR) (classified as A1 – A3) (Bikbov et al., 2020; Lewis et al., 2014; Webster et al., 2017). Table 1.1 below shows the classification of CKD based on both GFR and ACR.

Table 1.1: Classification of Chronic Kidney Disease (CKD) based on Glomerular Filtration Rate (GFR) and Albumin: Creatinine Ratio (ACR)

Classification based on GFR		**Classification based on ACR**		
Stages	Description and GFR (ml/min per 1.73m^2)	Normal to mildly increased (<30mg/g)	Moderately increased (30 to 300mg/g)	Severely increased (>300mg/g)
		A1	A2	A3
G1	Normal or high GFR >90	Patient will not be classified as having CKD	G1A2	G1A3
G2	Mildly decrease GFR 60 to 89		G2A2	G2A3

Table 1.1, continued

Classification based on GFR		Classification based on ACR		
Stages	Description and GFR (ml/min per 1.73m^2)	Normal to mildly increased (<30mg/g)	Moderately increased (30 to 300mg/g)	Severely increased (>300mg/g)
		A1	A2	A3
G3	Moderately decreased GFR 30 to 59	G3A1	G3A2	G3A3
G4	Severely decreased GFR 15 to 29	G4A1	G4A2	G4A3
G5	Kidney failure <15	G5A1	G5A2	G5A3

Note. Retrieved from "Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017" by B. Bikbov et al., 2020, *The Lancet, 395*(10225), p. 711.

Kidney failure is frequently underdiagnosed and undertreated because the kidneys are extremely adaptable, and as kidney function deteriorates, it can happen without evident signs and symptoms until a significant loss of nephrons has occurred (Lewis et al., 2014). The bodily system becomes progressively damaged when kidney function deteriorates.

Firstly, it will cause metabolic disturbances such as elevation of Blood Urea Nitrogen (BUN) and serum creatinine level. This elevation will cause the patient to developed fatigue, nausea, vomit, and headache (Lewis et al., 2014). Table 1.2 below shows normal value of BUN and serum creatinine.

Table 1.2: Normal Value of Blood Urea Nitrogen (BUN) and Serum Creatinine Level

Blood Urea Nitrogen (mg/dl)	Serum Creatinine Level (mg/dl)	
	Male	Female
5 to 20	0.6 to 1.2	0.5 to 11

Note. From *Medical-Surgical Nursing Assessment and Management of Clinical Problems* (9th ed., p 1702) by S. L. Lewis et al., 2014, Elsevier Inc., Copyright 2014 by Mosby.

Moreover, patient with kidney problem will have an insensitivity to the normal action of insulin which later will cause hyperglycemia and hyperinsulinemia (Lewis et al., 2014). The hyperinsulinemia increase production of triglycerides and this can contribute to increasing of cardiovascular disease in patients with kidney problems (Lewis et al., 2014).

Furthermore, kidney problem will affect the electrolyte and acid-base balance in the body which mainly involve the potassium and sodium. Reduction of potassium excretion will cause hyperkalemia in patient meanwhile reduction of sodium excretion by the kidney will cause sodium retention which later will contribute to the occurrence of edema, increase of blood pressure and risk for heart failure (Lewis et al., 2014). Apart from this, the patient may feel fatigued, easily irritated, and have mental ability alteration that is caused by electrolyte and acid-base imbalance in the body (Lewis et al., 2014; Webster et al., 2017).

Moreover, the hematologic system also will be affected as the kidney are responsible to produce hormone erythropoietin that is needed to produce red blood cell from bone marrow (Lewis et al., 2014). The reduction of hormone erythropoietin production will lead to anemia (Lewis et al., 2014).

Lastly, changes in urine output are also one of the common clinical manifestations that occurs among CKD patients such as polyuria when the concentrating ability of tubular is impaired, oliguria and nocturia due to renal sodium retention which lead to edema and proteinuria that is caused by loss of selectivity to protein filtration (Webster et al., 2017).

Chronic kidney Disease (CKD) is also resulted from various diseases that in the long period of time impaired the function and structure of the kidneys (Webster et al.,

2017). It is reported that the main risk factors and the most frequent comorbidities in CKD are diabetes mellitus (DM) and hypertension (HPT) (Ahlawat et al., 2016; Crews et al., 2019; Webster et al., 2017). Other less common causes of CKD are glomerulonephritis, cystic diseases, and urologic diseases (Lewis et al., 2014; Webster et al., 2017).

Along with the increase of other diseases, the prevalence rate of CKD also becoming apparently increasing all over the world. For example, in the Western countries such as Switzerland and Canada, the rate are at 10.4% (Hill et al., 2016; Tomonaga et al., 2013) and 12.5% respectively (Arora et al., 2013; Hill et al., 2016). In the United State, however, a substantially higher rate was reported (20.3%) (Gambaro et al., 2010). In Asian countries such as China, Singapore, India, and Thailand, prevalence rates were nearly same (10.8 percent, 12.8 percent, 17.2 percent, and 17.5 percent, respectively) (Hill et al., 2016; Ingsathit et al., 2010; Sabanayagam et al., 2010; Saminathan et al., 2020; Singh et al., 2013; Zhang et al., 2012). In 2017, each of Bangladesh, Indonesia, Japan, Pakistan, and Vietnam had more than 10 million cases of CKD (Bikbov et al., 2020).

The prevalence of CKD in Malaysia was within the reported rate as in other countries (Begum et al., 2016; Saminathan et al., 2020), with 9.07% in 2011 (Hooi et al., 2013; Ministry of Health Malaysia, 2018; Saminathan et al., 2020) and then increased to 15.5% in 2018 (Ministry of Health Malaysia, 2018; Saminathan et al., 2020). While in Hospital Universiti Sains Malaysia (USM), there were 6716 totals of CKD patients ranging from 2016 to 2019 (Unit Rekod Perubatan Hospital USM, 2019). Figure 1.1 below shows the incidence of CKD in Hospital USM from 2016 to 2019 and there was an increasing pattern of the incidence of CKD in year 2019 (25.96%) if compared to 2018 (20.87%).

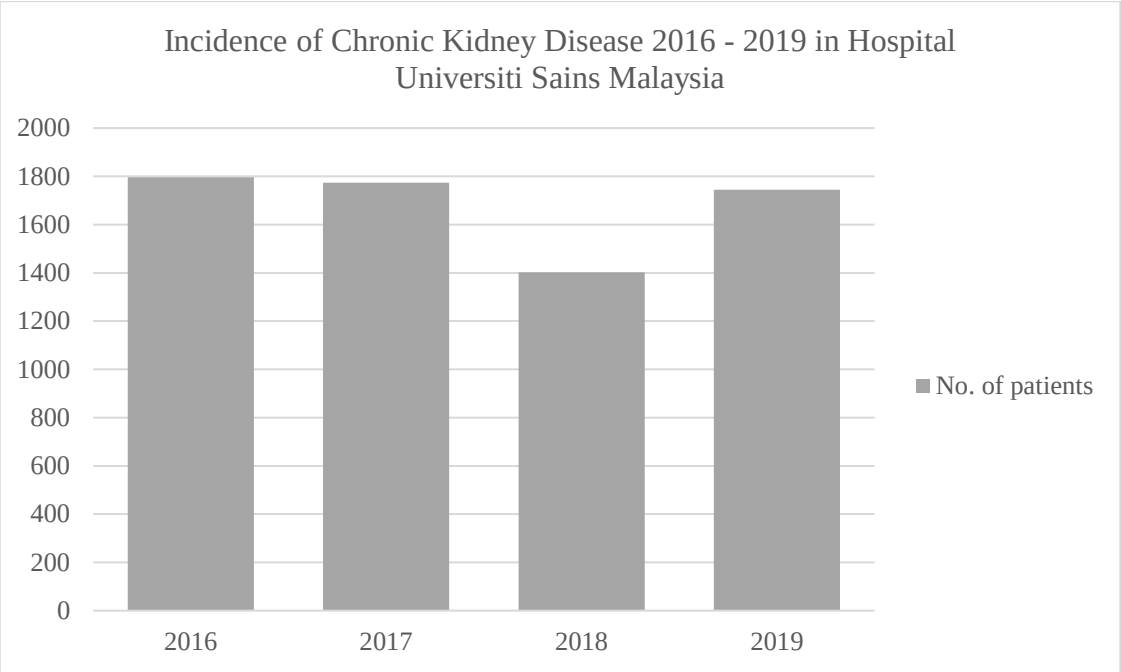


Figure 1.1: Incidence of Chronic Kidney Disease 2016 – 2019 in Hospital Universiti Sains Malaysia (Unit Rekod Perubatan Hospital USM, 2019)

It is acknowledged that CKD can rapidly progress along with other underlying disease and the treatment is often based on the disease process, the presence of underlying diseases, clinical manifestations and lab results such as BUN, serum creatinine and serum albumin (Arora et al., 2013; Lewis et al., 2014). The treatment is initially started with drug therapy and another less invasive treatment is needed in order to preserve existing kidney function, minimize the risks of cardiovascular disease, prevent complications, and ensure patient's comfort.

Chronic Kidney Disease (CKD) patients face several challenges, including poor quality of life, CKD complications, polypharmacy, and many others (Crews et al., 2019; Lewis et al., 2014; Webster et al., 2017). However, in this study, the researcher focuses more on CKD medication adherence. Indeed, many medications, such as anti-hypertension drugs, anti-diabetic drugs, diuretics, phosphate binders, statins, and iron supplements are prescribed for CKD patients to treat the clinical manifestations and

regulate the underlying condition like HPT and DM (Ahlawat et al., 2016; Lewis et al., 2014). However, when the GFR declining to less than 15 ml/min per 1·73 m², it indicates that she/he has reached the final stage (stage V), also known as End-Stage Kidney Disease (ESKD), which necessitates the use of an increasing number of medications (Lewis et al., 2014; Webster et al., 2017). Moreover, the main treatment options for ESKD patients are renal replacement therapy (RRT). For this therapy, the patient will be consulted to choose either for dialysis (hemodialysis or peritoneal dialysis) or kidney transplantation (Webster et al., 2017).

1.1.2 Medication Adherence

No doubt, compared to other chronic diseases, kidney failure patients must consume more medication it can reach more than 20 pills every day (Burnier et al., 2015). The key goals of these medications are to delay the progression by managing the underlying disease such as hypertension that can lead to further impairment of kidney function, to manage common complications of CKD that may speed up the degradation of kidney function such as hyperphosphatemia, acidosis or anaemia and also to identify, and manage comorbidities that can lead to the risk of mortality such as diabetes, coronary heart disease and heart failure (Burnier et al., 2015; Chandrasekhar et al., 2018).

Adherence to medication intake among CKD patients is very important to achieve the desired therapeutic outcome. The World Health Organization (WHO) defined medication adherence as "the extent to which a person's behaviour corresponds with the agreed recommendations of a healthcare provider in terms of taking medicines, following the recommended diet and/or executing lifestyle changes" (Ahlawat et al., 2016; AlKhattabi, 2014; Aminde et al., 2019; Burnier et al., 2015; Chandrasekhar et al., 2018; Chung et al., 2015; Nielsen et al., 2018). In contrast, non-adherence to medication is one of the key reasons that not only reduces the desired therapeutic outcome, worsen the

patient's health condition but also increase the patient's financial burden (Chandrasekhar et al., 2018). Undoubtedly, non-adherence to medication also has been reported as associated with increased mortality and hospitalizations in ESKD patients (Ghimire et al., 2015) and has contributed to many life-threatening complications (Ahlawat et al., 2016; Chironda & Bhengu, 2016).

1.1.3 Factors Associated with Non-Adherence to Medication

There are several factors associated to non-adherence to medication among CKD patients as indicated in the previous studies and official reports. The World Health Organization (WHO) has categorized the factors in five categories includes 1) sociodemographic (patient-related factors), 2) health care related factors, 3) therapy-related factors, 4) condition-related factors and 5) socioeconomic related factors (Chironda & Bhengu, 2016; Chung et al., 2015; Ghimire et al., 2017; Kadir et al., 2019)

Firstly is the sociodemographic (patient-related factors), it is further divided into other six sub-factors include the patient's age, gender, marital status, level of education, their awareness and attitude towards medications, self-efficacy, action control and facilitation (Ahlawat et al., 2016; Aminde et al., 2019; Chironda & Bhengu, 2016; Chung et al., 2015; Ghimire et al., 2017; Jain et al., 2018; Kadir et al., 2019; Saminathan et al., 2020).

Secondly is the health care related factors which include quality of interaction and trust between caregivers and patients, and availability of health facilities (Ahlawat et al., 2016; Aminde et al., 2019; Chironda & Bhengu, 2016; Chung et al., 2015; Ghimire et al., 2017; Jain et al., 2018; Kadir et al., 2019; Saminathan et al., 2020).

Thirdly is the therapy-related factors which include physical characteristics of medicines, packaging, and side effects that experienced by the patients (Ahlawat et al.,

2016; Aminde et al., 2019; Chironda & Bhengu, 2016; Chung et al., 2015; Ghimire et al., 2017; Jain et al., 2018; Kadir et al., 2019; Saminathan et al., 2020).

Fourthly is the condition-related factors, which refers to the underlying disease and symptom severity and lastly, the socioeconomic related factors such as income status, employment status, access to medicines, and relative affordability (Ahlawat et al., 2016; Aminde et al., 2019; Chironda & Bhengu, 2016; Chung et al., 2015; Ghimire et al., 2017; Jain et al., 2018; Kadir et al., 2019; Saminathan et al., 2020).

The current study focuses on selected sociodemographic (patient related factors) characteristics which are age, gender, ethnicity, education level and the number of medications intake daily. This will be discussed further in Chapter 2 Review of Literature, Section 2.2.3 Sociodemographic Factors Associated with Non-Adherence to Medication.

1.2 Problem Statement

In 2017, 697.5 million cases of CKD were reported globally (Bikbov et al., 2020), posing a significant financial and disease burden on healthcare systems around the world (Ahlawat et al., 2016). According to Global Burden of Disease report from 2015, CKD is the leading cause of death compared to other diseases such as cardiovascular diseases, cancer, chronic respiratory diseases, and diabetes (Crews et al., 2019).

This situation becomes increasingly burdensome with the non-adherence to medication among patients. WHO stated that poor medication adherence can be a "worldwide problem of striking magnitude" (Conn et al., 2016), in which the prevalence rate of non-adherence to medication at 78% would significantly increase the disease burden, and severely decreased the patient quality of life (Ahlawat et al., 2016). Although many interventions have been done to aid in controlling the disease, the medication

adherence in a patient with CKD is challenging for most (Burnier et al., 2015; Jain et al., 2018).

Based on the researcher literature search, study on non-adherence to medication among CKD patients is very limited. Furthermore, most of the existing studies do not sufficiently provide the prevalence and factors associated with non-adherence to medication among CKD patients although this issue has long been the interest of researchers worldwide (Chandrasekhar et al., 2018; Dempster et al., 2018; Jain et al., 2018). The recent data on this issue can help resolve to identify problem that cause the non-adherence to medication among patients.

Furthermore, by identifying the factors that contribute to non-adherence, it will act as the building block to manage the problem (Chironda & Bhengu, 2016), as well as helps to recognize the adherence obstacles, establish, and validate intervention measures to encourage adherence to medication among patients (Ghimire et al., 2015).

All these issues in mind have triggered the researcher to conduct a study with the aim to assess non-adherence to medication among CKD patients in Hospital Universiti Sains Malaysia (USM).

1.3 Research Questions

i. What is the prevalence of non-adherence to medication among CKD patients in Hospital USM?
ii. What is the satisfaction level of CKD patient on medication information provided by health professionals (doctor, nurses, and pharmacists) in Hospital USM?
iii. What is the factor associated with non-adherence to medication among CKD patients in Hospital USM?

1.4 Research Objectives

1.4.1 General Objective

To assess medication adherence among CKD patients in Hospital USM.

1.4.2 Specific Objectives

i. To determine the prevalence of non-adherence to medication among CKD patients in Hospital USM.

ii. To assess the CKD patients' satisfaction level on medication information provided by health professionals (doctor, nurses, and pharmacists) in Hospital USM.

iii. To identify the factor associated with non-adherence to medication among CKD patients in Hospital USM.

1.5 Research Hypothesis

i. Null Hypothesis (H_0): There is no significant association between the sociodemographic factors (age, gender, ethnicity, educational level, and number of medications intake daily) with non-adherence to medication among CKD patients in Hospital USM.

ii. Alternative Hypothesis (H_a): There is a significant association between the sociodemographic factors (age, gender, ethnicity, educational level, and number of medications intake daily) with non-adherence to medication among CKD patient in Hospital USM.

1.6 Significance of the Study

Although many interventions have been implemented across the world to slow the progression of CKD, medication adherence among patients remains a concern that requires full attention from healthcare providers. This study's findings have a substantial impact on the hospital, health professionals (doctors, nurses, and pharmacists), and,

finally, patients in Hospital USM. In general, identifying the prevalence and factors associated with non-adherence helps to assist in better healthcare planning that is suitable for the factors identified and resource allocation for specific planning done for CKD (Kadir et al., 2019; Saminathan et al., 2020). This research is also beneficial to healthcare administrators in developing policies and strategies to improve the overall quality of healthcare services. Furthermore, this study encourages healthcare professionals to start a conversation with their patients about medication concerns (Ghimire et al., 2017) which strengthen the healthcare professional-patient interaction. Lastly, it also gives a significant benefit to the patient because this study able to provide some clues and new perspectives on how medication adherence could be addressed and possibly improved (Burnier et al., 2015).

1.7 Conceptual and Operational Definitions

Table 1.3: Conceptual and operational definitions of the study

	Conceptual Definitions	Operational Definitions
Chronic Kidney Disease (CKD)	Kidney damage or when the function of kidney reduces with a glomerular filtration rate (GFR) of less than 60 millilitres/minutes (ml/min) per 1.73 square meter (m2) or a kidney damage marker of at least three months, irrespective of the underlying cause (Jain et al., 2018; Verma et al., 2018; Webster et al., 2017).	In this study, patients diagnosed with CKD regardless of the stages were included as the subject of this study.
Chronic Kidney Disease (CKD) patients	Patient with GFR <60 ml/min per 1.73m2 or if patient with GFR >60 ml/min per 1.73m2 but have another kidney damage marker (Webster et al., 2017).	In this study, patients at *Klinik Pakar Perubatan* and at Chronic Kidney Disease Resource Centre, Hospital USM diagnosed with CKD and fit with inclusion criteria were the respondent in this study.
Medication adherence	The extent to which a person's behaviour corresponds with the agreed recommendations of a healthcare provider in terms of taking medicines, following the recommended diet and / or executing lifestyle changes (Ahlawat et al., 2016; AlKhattabi, 2014; Aminde et al., 2019; Burnier et al., 2015; Chandrasekhar et al., 2018; Chung et al., 2015; Nielsen et al., 2018).	In this study, medication adherence of CKD patient towards prescribed medication were assessed.
Prevalence	Proportion of both new and pre-existing health conditions, illness, and disease in the population at specified time (Carroll, 2013).	In this study, the researcher aims to determine the prevalence of non-adherence to medication among CKD patients in Hospital USM.
Satisfaction level	The outcome of a psychological mechanism in which the consumer blends his perceptions and emotions with expectations and perceived value after consumption of a product or service (Biesok & Wyród-Wróbel, 2011).	In this study, the patient's satisfaction level on medication information provided by health professionals (doctor, nurses, and pharmacists) in Hospital USM were assessed.

CHAPTER 2 REVIEW OF LITERATURE

2.1 Introduction

This chapter reviews the current literature related to medication adherence among Chronic Kidney Disease (CKD) patients in terms of the prevalence of non-adherence to medication, satisfaction level of patient on medication information provided by health professionals (doctor, nurses, and pharmacists), and factors associated with non-adherence to medication. In additions to this, theoretical framework that was used to guide this study is also included.

2.2 Review of Related Literature

2.2.1 Prevalence of Non-Adherence to Medication

In an intervention study done in India, it was indicated that 91.4% of patients from stage III to V were not adhere to medication. Following the intervention, there was a reduction of 57% in non-adherence (Chandrasekhar et al., 2018). Whereas in other study conducted in India among CKD patients 29% of stage I – III, 27% of stage IV and 44% of stage V, the prevalence rate of non-adherence to medication was reported at 78% (Ahlawat et al., 2016). This showed that, the higher the stages of CKD among patients, the higher the non-adherence to medication. Complexity of prescribed medication and polypharmacy among patient with advanced stage led to negative outcome on the patient such as higher non-adherence.

While in Malaysia, a study was done in ten hospitals and non-adherence to medication was reported at 17.7% based on overall assessment. However if assessed individually, the prevalence of non-adherence was higher (72.5%) (Kadir et al., 2019). Obviously, strict individual assessment provides a better evidence on the prevalence of

non-adherence. Moreover, 73.5% of the respondents in this study were in stage V, which lead to a more complex management on their conditions.

Apart from this, there were few studies looking at non-adherence to medication without specifying the stages of CKD. For example, in a study by Sontakke et al. (2015), it was reported that non-adherence rate was 37.3% among CKD patients. Meanwhile in other study, 58% non-adherence to medication was report and this rate had gradually increased to 82% at two years follow up (Verma et al., 2018). Both of these studied showed high prevalence of medication non-adherence among CKD patients.

Furthermore, the prevalence of non-adherence to medication was also indicated at 12.01%, 20.1% and 56.7% among patients receiving haemodialysis in Makkah (AlKhattabi, 2014; Ghimire et al., 2017; Ozen et al., 2019). While in a systematic review by Ghimire et al. (2015) on 44 articles from 1970 to 2014, they reported the prevalence ranged between 12.5% to 98.6%. All these findings showed that although medication adherence is an essential component to effectively control the diseases, this therapeutic goal however, is difficult to achieve due to other related factors. Some of the common factors reported were rigorous weekly schedule of dialysis sessions, increased number or dosage of medicines along the course of the patient's disease, and medication regimen that is difficult for the patients to follow (Burnier et al., 2015; Ghimire et al., 2015). These situations will later lead to higher number of non-adherences to their treatment, especially on medication.

2.2.2 Patient's Satisfaction Level on Medication Information

Intentional non-adherence according to Cedillo-Couvert et al. (2018) is associated with increased risk of CKD progression because the patient tends to purposefully be missing out or adding in an extra pill. It is believed that most of the patient with this

behaviour were more likely to have a poor relationship with health professional especially nurses, doctors, and pharmacist. In line with that, patients who feel that their physicians communicate well and actively encourage them in self-care tends to be more motivated to adhere compared to those who do not received such treatment from the health professionals (Chironda & Bhengu, 2016).

Nonetheless, it was reported that there were higher number of respondents (77.1%) who were satisfied with the pharmacist's consultation during their visit at the pharmacy where the pharmacist delivered their medicines in a polite way and the instructions and information were clearly labelled and explained for each medication (El-Sharif et al., 2017). Furthermore, Nasir et al. (2018) reported that those with higher interaction with the physician and satisfied with the information shared by the physician was 1.2 times more likely to report full adherence in medication.

Patients' satisfaction level towards nurses, however, was different compared to other group of health professionals. For example, Karaca & Durna (2019) reported a higher patients' satisfaction level on "Concern and Caring by Nurses" but lower satisfaction level was indicated on the information given by the nurses regarding their condition and treatment. These findings revealed that the satisfaction level of patient towards information given by health professional has a great influence on their adherence to medication.

2.2.3 Sociodemographic Factors Associated with Non-Adherence to Medication

There are several factors associated with non-adherence to medication among CKD patients as reported in the literature. However, as mentioned in Chapter 1, (Section 1.1.3), the researcher only focused on selected sociodemographic (patient related factors) characteristics. While all the other related factors (socioeconomic, health care, therapy,

and condition related factors) were not covered in this proposed study due to time and financial constraints. All the selected sociodemographic characteristics factors are discussed further in the following sections.

2.2.3.1 Age

In term of age, younger age was found as associated with low adherence to medication (Cedillo-Couvert et al., 2018; Chironda & Bhengu, 2016). It is also reported that older people were more likely to be adherent toward medication (Kadir et al., 2019). A contrast findings was indicated in India, when they reported that elderly patient had higher prevalence on non-adherence to medication (Ahlawat et al., 2016). Apart from that, few studies also have reported non-adherence to medication in the older population (Ahlawat et al., 2016; Ghimire et al., 2015; Mukhtar et al., 2014). The differences in the result presented in the previous studies shows the reasons for non-adherence to medication. Kadir et al. (2019) suggested that older people had better adherence towards medication because they are more familiar with their disease and condition. Moreover, the frequent visit to the hospital also allows them to be more familiar with the regime and they had more free time if compared to younger age. These statements are also supported by Nielsen et al. (2018) when they are associating younger age with a non-adherence to medication due to their busy daily schedule and caused them delaying medication intake in order to do other things that is more important. Hence, forgot to take medication. Nevertheless, older age was also found as associated with non-adherence to medication because of low understanding on complex therapeutic regimen and about their diseases as reported by Ahlawat et al. (2016).

2.2.3.2 Gender

When compared to male, female was found as significantly associated with non-adherence to medication. Similarly, studies done by Ozen et al. (2019) and Cedillo-

Couvert et al. (2018) also reported that female were significantly associated with non-adherence to medication. Furthermore, the similar results were indicated in a study done in Malaysia with the prevalence of non-adherence to medication was 73.4% in the female group (Kadir et al., 2019) and in Ahlawat et al. (2016) with 62.3% of female did not adhere to medication.

2.2.3.3 Ethnicity

In terms of ethnicity, a study by Kadir et al. (2019) among 491 CKD patients in Malaysia found that the prevalence of non-adherence to medication based on the three main races was as follows: Malay (73.7%), Chinese (69%) and Indian (73.7%). Moreover, a study conducted by Cedillo-Couvert et al. (2018) found that Non-Hispanic Black or Hispanic have higher prevalence of non-adherence to medication and similarly, studies conducted by Ghimire et al. (2015) and Patzer et al. (2016) also reported that a minority ethnic patient were associated with low adherence to medication.

2.2.3.4 Educational Level

According to a study done in four Haemodialysis Centre in Turkey, 54.6% of the patients with primary school background did not adhered to medication (Ozen et al., 2019). This shows that education level influences adherence to medication. Similar result was also reported in the other three studies that lower education level was found as significantly associated with non-adherence to medication (Ahlawat et al., 2016; Chironda & Bhengu, 2016; Patzer et al., 2016). Moreover, a study conducted by Kadir et al. (2019) also found that people with higher drug knowledge had better adherence by 8.8 times compared to people with lower drug knowledge. Not only low education have poor correlation towards knowledge of the disease and treatment (Chironda & Bhengu, 2016), but it will lead to lack of understanding on the medication indication and effects (Nielsen et al., 2018). Hence, lack of understanding will affect their adherence towards medication.

2.2.3.5 Number of Medications Intake Daily

Increase number of medication prescribed were significantly associated with non-adherence among patients as reported in three studies (Ahlawat et al., 2016; Ghimire et al., 2015; Kadir et al., 2019). Higher daily intake of medications can negatively influence the patient's perception towards medication, which later on may reduce their adherence towards the medication due to concerns about side effects and long-term adverse effects of polypharmacy (Ghimire et al., 2015; Nielsen et al., 2018).

2.2.4 Reasons for Non-Adherence to Medication

Apart from the factors that was already mentioned above, there are other possible causes of non-adherence to medication among CKD patients. This includes forgetfulness, too busy, high medication cost and lack of finances, disappearances of symptoms, lack of information, complex dosing schedule, missed appointment and poor access to medication (Ahlawat et al., 2016; Aminde et al., 2019; Verma et al., 2018).

2.3 Theoretical Framework

The theoretical framework that was used to guide this study is Social Cognitive Theory by Albert Bandura (1986). It is the most common theories and models use in medication adherence intervention research (Conn et al., 2016). Measurement of medication adherence is challenging because it depends on individual patient behaviour (Jain et al., 2018) and Social cognitive theory proposes that behaviour is affected by multiple influences including environmental and personal factors, and aspects of the behaviour itself (Chisholm-Burns & Spivey, 2010). Bandura explained that a central concept of Social Cognitive Theory is that health behaviour is a reciprocal interaction between environmental factors, cognitive factors and behavioural factors (Amico et al., 2018; Chin & Mansori, 2018; LaMorte, 2019).

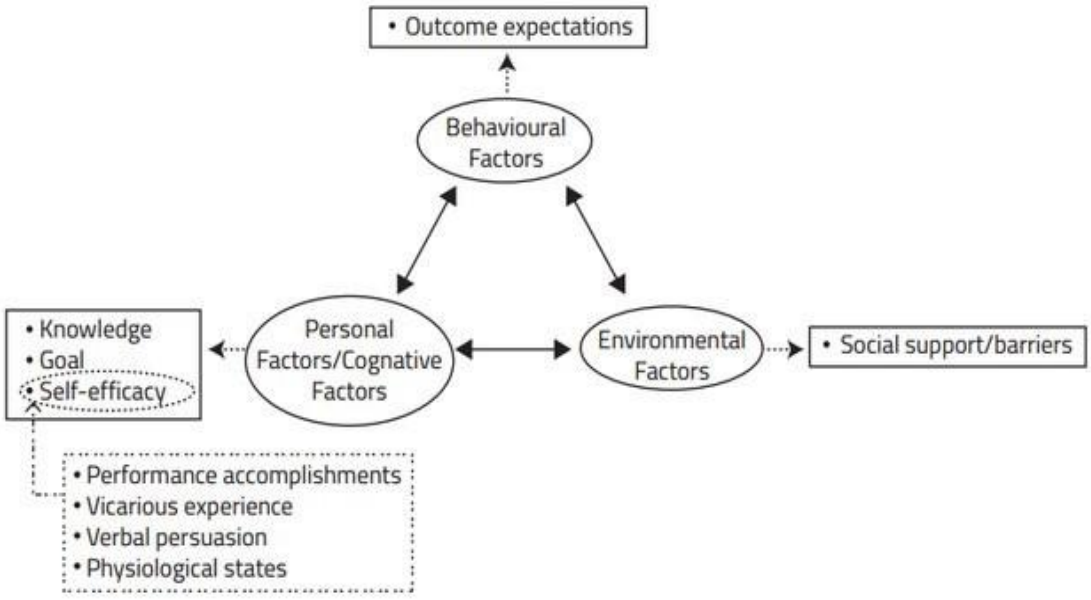


Figure 2.1: Determinants of Social Cognitive Theory

The environmental factor includes stimuli from surrounding environment such as social support from family members which reinforce them to adopt or avoid the adherence (Amico et al., 2018; Chin & Mansori, 2018; LaMorte, 2019). While for cognitive factors, it includes attitudes, beliefs, expectations about outcomes and self-efficacy that is significantly influenced by performance accomplishments, vicarious experience, verbal persuasion, and physiological states (Amico et al., 2018; Chin & Mansori, 2018; LaMorte, 2019). Lastly, behavioral factor that is influence by their self-observation and judgment on the outcome expectation which would motivate them to repeat the behavior if they perceived a similar reward (Amico et al., 2018; Chin & Mansori, 2018; LaMorte, 2019). Figure 2.2 illustrate the adopted Social Cognitive Theory used in this research study.

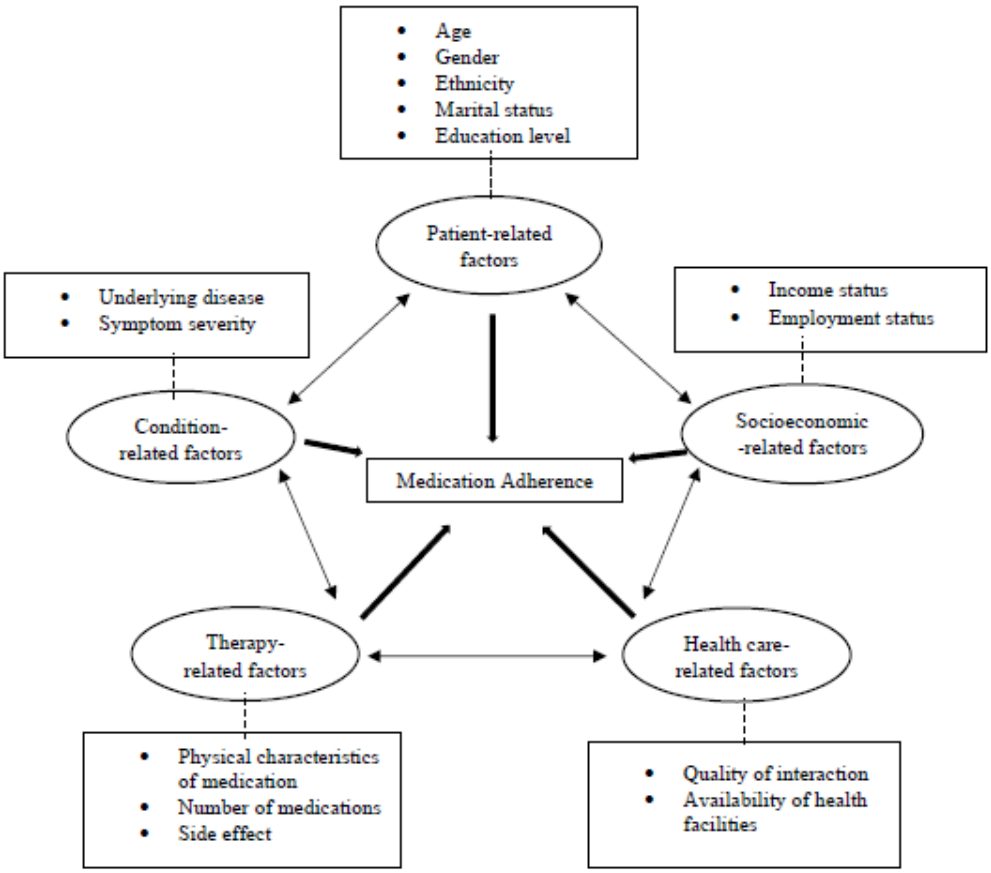


Figure 2.2: Conceptual framework of study

Figure 2.2 shows the behaviour elicits by the patient is resulted from a reciprocal interaction between factors. Patient related factors are reciprocating with the condition related factors for example, patient with advanced age will have higher occurrence of other underlying disease. By the same token, underlying disease will definitely increase the number of medications daily. High number of medications with different side effect will later on will cause the side effect to outweigh the therapeutic effects of medication and patient will be prone to not taking their medication for that reason (Nielsen et al., 2018).

Moreover, the quality of interaction between the patient and health professionals will affect the patient's perception and knowledge on medication. This later will give impact to the behaviour of patient in medication adherence. For example, patient with good interaction with health professional will be able to be involved in decision making such as they will definitely be able to discuss regarding the side effect and the physical characteristics of the medication which suits their lifestyle preferences (Nielsen et al., 2018). Hence, better involvement in decision regarding medication will increase adherence of medication among CKD patients. That is why the interaction between health professionals and patients are important.

Other than that, the patient's income and employment status can affect the patient's adherence to medication. As stated by Nielsen et al. (2018), patient with low income will have difficulty to buy their own medication. Apart from this, the availability of facilities near the patients also can give impact to the patients' adherence especially if the patient has financial burden, it will be difficult for them to go to the hospital or clinic if the facilities are difficult to reach. Lastly, in relation with the patient related factors, most patient with higher level of education will have higher income since they were able to secure a better job (Wright & Horta, 2018). Thus, with higher income and educational level, the patients will have high adherence to medication since they are able to buy their medication without any difficulties and have better understanding on medication being prescribed by health professionals.

Therefore, Social Cognitive Theory is used as a guide in this study because medication adherence among CKD patients were reportedly have few related factors as discussed above that reciprocate with each other and later influenced the level of patient's adherence to medication.

CHAPTER 3 METHODOLOGY

3.1 Introduction

This chapter stated the research methods and statistical analysis of the data. The details on research design, location, duration, population, instrument, variables, data collection plan and ethical consideration are included in this chapter. Other than that, the study flow chart on the data collection is also presented at the end of this chapter.

3.2 Research Design

In this study, a cross sectional survey was used. Cross-sectional study can be defined as the outcome and exposure in the study respondents is measured at the same time by the researcher (Setia, 2016).

3.3 Study Setting and Population

This study was conducted at *Klinik Pakar Perubatan* (KPP) and at Chronic Kidney Disease (CKD) Resource Centre, Hospital USM, Kubang Kerian, Kelantan. Every Sunday and Tuesday, KPP schedule a clinic for CKD patients. Meanwhile, every Wednesday at the CKD Resource Centre is scheduled for CKD patients. The study population was selected among CKD patients that came to KPP as well as at CKD Resource Centre, Hospital USM for routine follow-up and other related management. They were selected based on the inclusion and exclusion criteria as the following.

3.4 Sampling Plan

Sampling can be referred as a process of selecting several subjects from a target population as a research respondent (Piaw, 2016). Selecting a suitable sample will increase the validity and reliability of the research.

3.4.1 Sample Criteria

3.4.1.1 Inclusion Criteria

i. Male and female patients diagnosed with CKD and receiving treatment more than one year in Hospital USM.

ii. Aged 18 years old and above.

iii. Able to understand and speak in Bahasa Malaysia.

iv. Agreed to participate in the study.

3.4.1.2 Exclusion Criteria

i. Patients with cognitive impairment which may limit their ability to participate.

ii. Patients that are unable to complete the questionnaires.

3.4.2 Sample Size Estimation

Sample size for this study were calculated according to the research objectives. Following that, the exact sample size was finalized by considering the one with the largest number.

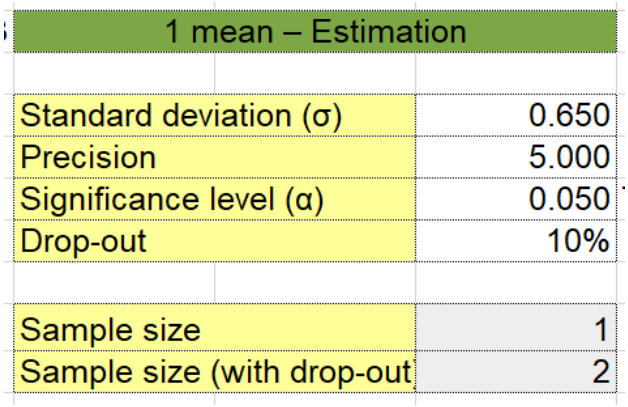
i. Sample size for the first objective was estimated using single proportion and Sample Size Calculator (Naing, 2003) was used to get samples with high accuracy as the following:

1 proportion – Estimation	
Proportion (p)	72.50%
Precision	8.00%
Significance level (α)	0.050
Drop-out	10%
Sample size	120
Sample size (with drop-out)	134

Figure 3.1: Sample size calculation using single proportion

The proportion of 72.5% was obtained from the previous study (Kadir et al., 2019). A sample size of 120 was recommended and the adjusted sample size after considering 10% of dropout was 134.

ii. Sample size for second objective was estimated using a single mean which then calculated using Sample Size Calculator (Naing, 2003). The calculation is shown in Figure 3.2 below:



1 mean – Estimation	
Standard deviation (σ)	0.650
Precision	5.000
Significance level (α)	0.050
Drop-out	10%
Sample size	1
Sample size (with drop-out	2

Figure 3.2: Sample size calculation using single mean

The standard deviation of 0.65 was obtained from the previous study (Karaca & Durna, 2019). Because of the sample size was too small, it was not taken into consideration in this study.

iii. Sample size for the third objective was estimated using multiple and simple logistic regression and each of the variables was calculated using double proportion (Lemeshow et al., 1990) because all of the outcome variables were categorical (Two groups: Low medication adherence and high medication adherence). The calculation was shown below: