

CHAPTER 1

INTRODUCTION

1.1 Background

Diabetes Mellitus (DM) is a group chronic metabolic disease that is characterised with elevated levels of blood glucose that results from defects in insulin secretion, insulin action, or both (American Diabetes Association, 2010). The suspicion of DM needs to be considered if there are signs of classic complaints of DM such as polyuria, polydipsia, polyphagia, and unexplained weight loss. Other complaints that could be considered are weakness, paresthesia, blurred vision, erectile dysfunction in men, and pruritus vulvae in women (Perkumpulan Endokrinologi Indonesia, 2011). The criteria that could be used in diagnosis of DM are fasting plasma glucose (FPG) ≥ 126 mg/dL, 2-h PG ≥ 200 mg/dL, random plasma glucose ≥ 200 mg/dL with symptoms of hyperglycemia, or HbA1C level of $\geq 6.5\%$ using method that is National Glycohemoglobin Standardization Program (NGSP) certified and standardized (American Diabetes Association, 2020).

International Diabetes Federation (IDF) estimated that in 2019, 463.0 million adults aged 20–79 years worldwide suffer from diabetes with the global prevalence counted to 9.3%. By the year of 2030 the cases are expected to increase to 578.4 million with global prevalence of 10.2%. IDF statistics show Indonesia was ranked 7th amongst the top ten countries with the highest number of people with diabetes in 2019. In Indonesia the prevalence of DM among the population with age of ≥ 15 years old by diagnosis of doctor increased from

1.5% in 2013 to 2% in 2018 (Kemenkes RI, 2018). The total diabetes-related health expenditure of Indonesia in 2019 accounted for US\$3,901.2 million whereas the mean diabetes-related health expenditure per person accounted for US\$365.2 (International Diabetes Federation, 2019).

The main pathophysiology of type 2 diabetes mellitus is classically associated with the triumvirate of impaired insulin secretion, insulin resistance in muscle and liver, and elevated hepatic glucose production (HGP). However, with additional mechanism of the fat cell (accelerated lipolysis), gastrointestinal tract (incretin deficiency/resistance), α -cell (hyperglucagonemia), kidney (increased glucose reabsorption), and brain (insulin resistance), all these defects combined play a major part in the development of glucose intolerance and usually referred as ominous octet (DeFronzo, 2009). Hence to manage T2DM with the lying pathophysiology in mind, usually multiple drugs are used in combination.

The diagnosis of diabetes is usually accompanied with additional comorbid conditions that may complicate the patient's self-management (Kerr, 2007). To add, there are long-term complications of diabetes that include retinopathy with the probability of vision loss, nephropathy that leads to renal failure, peripheral and autonomic neuropathy, cardiovascular symptoms, and sexual dysfunction (American Diabetes Association, 2014). Factors mentioned above that lead to use of many combinations of medicines often result to polypharmacy in T2DM patient treatment. Where T2DM patient would need additional therapeutic agent in each increase of comorbidities presence leading to additional

prescription of drugs (Dobrică, 2019). The common presence of polypharmacy in diabetes mellitus patient could be seen in several previous study. A study conducted in Saudi Arabia showed that of all the participant nearly 78% of them had prescription of polypharmacy (Alwhaibi, 2018). Other study conducted in China also shows similar result, where of all the T2DM subjects, 72.2% had prescription of polypharmacy (Li, 2020). Hence multifactorial medication used to treat a diabetes patient with additional complications and complexity of treatments may have influence on adherence (García-Pérez, 2013).

The classic treatment target of T2DM is adequate glycemic control, however at least 45% of patients failed to achieve it, with medication adherence as one of the main contributing factors (Polonsky et al., 2016). Adherence is important in T2DM patients, where poor adherence to medication itself is likely to be associated with inadequate glycemic control, increased morbidity and mortality, hospitalization, and complication of diabetes (Polonsky, 2016).

The problems of poor adherence in diabetes patients are widely spread and have been long recorded in several previous study. In previous study, a meta-analysis of 569 studies of adherence across a range of medical disorders was conducted and the average adherence rate for diabetes was presented among the lowest (DiMatteo, 2004). A literature review of 139 studies reporting adherence data of cardiovascular and antidiabetic medication by Cramer in 2008 showed that only 58% of patients had OADs medication for more than 80% of their days ‘on therapy’ in the year (Cramer, 2008). In accordance, a research conducted in one of the Primary Health Care Center in Surabaya

(Kedurus) by Rosyida showed that of all the subjects only 18.20% had a high adherence, 24.20% had a medium adherence and 57.60% had a low adherence to their OAD medications (Rosyida, 2015). Also, another case of control study was conducted in three Primary Health Care Center in Surabaya (Mojo, Pucang Sawu, and Keputih) and showed that of all the diabetes patient with category of unregulated blood glucose, only 46.2% are adherent and the rest 53.8% are not adherent, meanwhile for the regulated blood glucose category 92.3% were adherent and 7.7% were not adherent in consuming anti-diabetic drugs (Nanda, 2018).

Adherence itself could be perceived as the extent of the patient's willingness to comply with managements recommended by the health care provider. Based on WHO reports on multi-factorial of nonadherence to long-term therapies, the variables that could be considered to correlates with adherence in diabetes patient are treatment and disease characteristics (complexity of treatment, duration of disease and delivery of care) , intra-personal factors (age, gender), inter-personal factors (patient-provider relation and social support), and environmental factors (World Health Organization, 2003). Strategy that could be used to face poor adherence in T2DM patients is by identifying specific obstacles to medication adherence that are potentially modifiable and focusing on reducing medication burden is of example (Polonsky, 2016). Hence, the complexity of medication regimens and pill burden may be considered as variables that could affect adherence and are modifiable (Böhm, 2021).

The complexity of a medication regimen could be simply defined as the number of drugs and the dosing frequency however some perceived that dosing forms and additional instruction are also part of it (Ayele, 2019). Research in general showed that the probability of adherence decreases with increasing treatment complexity (Curkendall, 2013).

Pill burden or often referred as total daily pill burden is the total number of pill that patient take daily and it is determined by counting the number of orally administered pills, tablets, or capsules taken for both blood glucose control therapy and treatment of associated conditions per day (BlüHerMatthias, 2015). Several studies between adherence to OAD medications and pill burden on T2DM patient have been conducted in several countries. The first study of T2DM patients adherence in a complete population performed by Donnan in Scotland showed that the number of tablets is considered as a factor where poorer adherence was observed with each increase in the daily number of tablets taken and increase of co-medications (Donnan, 2002). Following that, previous study of pill burden on T2DM patients in Germany conducted in 2015 also showed that a high pill count in antidiabetic therapy constitutes a large burden for T2DM patients, where 52.2% from all of the subjects were taking three to six tablets per day (55.6% of it were <65 years of age and 48.9% were ≥ 65 years of age) (BlüHerMatthias, 2015). However, a study of determinants of adherence to oral antidiabetic medications in U.S. adults with T2DM showed that total pill burden were positively related to adherence, where each additional pill a patient took per day the adherence to antidiabetic medications increased by 22% (Kirkman, 2015).

Several previous studies of factors affecting treatment adherence to diabetes medication in Indonesia have explored medication burden and the associated variables. However, studies of associated variables on the medication burden in Indonesian that is currently available, mostly focuses only on daily number of drugs. Studies that focus on total daily pill burden for both diabetes and non-diabetes treatment that are specified in T2DM patients in Indonesia have not been widely explored yet. Surabaya is chosen for collecting the data for this research since East Java is ranked as one of the provinces with highest number of diabetes patients in Indonesia (Kemenkes RI, 2018) and Dr. Soetomo General Academic Hospital where this study is going to be carried out is considered as top referral for East Java and Eastern region of Indonesia.

This research aimed to study the correlation between total daily pill burden of various treatment and adherence of T2DM patient in endocrine outpatient clinic of Dr. Soetomo General Academic Hospital in Surabaya, East Java, Indonesia.

1.2 Problem Formulation

Are there any correlation between total daily pill burden of various treatment and adherence in type 2 diabetes mellitus patients?

1.3 Research Objectives

Based on the above problem formulation, the purpose of this research is to: -

1.3.1 General Objective

To analyze the correlation between total daily pill burden of various treatment and adherence in type 2 diabetes mellitus patients.

1.3.2 Specific Objective

- a) To identify the general characteristics distribution among T2DM patients.
- b) To identify the distribution of various treatment in T2DM patients.
- c) To identify the data of total daily pill burden in T2DM patient.
- d) To identify the treatment adherence to medication of OAD in T2DM patients.
- e) To analyze the correlation between total daily pill burden and adherence to OAD medication of T2DM patients.
- f) To analyze the correlation between educational level and adherence to OAD medication of T2DM.
- g) To identify the data distribution behind the reasons for nonadherence to OAD medication of T2DM patients.

1.4 Research Benefits

1.4.1 Theoretical Benefit

To further update the knowledge on the correlation between total daily pill burden of various treatment and adherence in type 2 diabetes mellitus patients, and the possible reasons for nonadherence.

1.4.2 Practical Benefit

The knowledge on the correlation between total daily pill burden of various treatment and adherence in type 2 diabetes mellitus patients and the reasons for nonadherence could be used by health practitioners as a reference in considering the therapy choice for T2DM patients. Could be considered by health practitioners as a reference regarding Hospital Health Promotion/ PKRS (Promosi Kesehatan Rumah Sakit) in counseling T2DM therapy adherence to patients.