CHAPTER 1

INTRODUCTION

1.1 Background

Nowadays, lots of people are interested in consuming ketogenic diet because it helps to manage their weight, especially to lose weight. Besides weight loss, ketogenic diet is also very useful for controlling blood sugar level, decreasing serum triglycerides, treating cancer, alzheimer, as well as epilepsy, since it was the main purpose of developing ketogenic diet (Mohan and Shilpa, 2018). Ketogenic diet contains of high fat with low carbohydrate and adequate protein so that our body will digest fat more than carbohydrate. This high-fat diet aims to activate ketogenesis to break down the fat into fatty acids and ketone bodies. Then, ketone bodies cross the blood-brain barrier to provide energy for our brain (Kalra et al., 2018). Based on the ratio of fat to carbohydrate and protein, there are 4 types of ketogenic diet. They are classic ketogenic diet, medium chain triglycerides (MCT) diet, modified atkins diet (MAD), and low gycemic index treatment (LGIT) (Williams and Cervenka, 2017).

According to WHO (2019), cancer is the second leading cause of death in the world, about 1 in 6 deaths is caused by cancer. It has been reported that an increase in number of new cases until 18.1 million, and number of deaths until 9.6 million in 2018 in worldwide. While in Indonesia, there were 348.809 new cases and 207.210 deaths in 2018. Based on those, cancer is considered as one of several serious problem.

There are lots of factors that can increase the risk of cancer, such as age, alcohol, chronic inflammation, obesity, radiation, immunosuppressant, infectious agent and etc (National Cancer Institute, 2015). Besides those all, there are still some more other factors that can cause cancer, and not all of the factors can be prevented. Some preventions can be done, by reducing carcinogenic exposure and do healthy diet in order to maintain our body weight. It is said that ketogenic diet can help to prevent cancer, but the detail mechanism is still unknown yet (Kamińska et al., 2015).

Chronic inflammation has been associated as early progression of cancer. As malignancy develop, it requires numerous inflammatory cells to favor what they need to stay and grow. Excess number of leucocytes and phagocytic cells can give rise to DNA damage. Moreover, if this recurs, it can result in gene mutation (Coussens and Werb, 2002).

Bcl-2 is a family protein which gene is located in chromosome 18, its role is to control a cell to stay alive or to die by blocking apoptosis. In malignancy, Bcl-2 gene is transferred to different chromosome, which explains why Bcl-2 is found in large amount and how cancer cells can survive from dying (National Cancer Institute, 2019). Bcl-2 expression increases by avoiding apoptosis which helps oncogenic transformation, so that will explain the unstoppable growth of tumor, and resistance to therapy. There are some mechanisms of upregulation of Bcl-2, chromosomal translocation, gene amplification, and increase gene expression (Campbell and Tait, 2019).

Ketogenic diet may affect cancer growth allegedly through a decrease in progesterone and lead to Akt activation failure. This inactivate Akt is expected to

reduce Bcl-2 expression and induce apoptosis (Andrade et al., 2014, Rhodes et al., 2005 and Daniel et al., 2011).

To determine the effect of ketogenic diet on the expression of Bcl-2 as suppressor of cancer cell growth, a systematical review will be conducted. By the end of this review, Bcl-2 levels will be examined as an apoptosis marker of cancer.

1.2 Research Question

1. Is there any changes in Bcl-2 expression as an apoptosis marker of cancer?

2. Can ketogenic diet be used as cancer prevention?

1.3 Research Objectives

1.3.1 General Objective

To find out the effect of ketogenic diet on Bcl-2 expression in cancer.

1.3.2 Specific Objectives

1. To find out if there is any changes in Bcl-2 expression as an apoptosis marker of cancer.

2. To find out if ketogenic diet can be used as a prevention of cancer.

1.4 Research Benefits

1.4.1 Theoretical Benefit

To improve new knowledge about factors that can slow down the growth of cancer cells.

1.4.2 Practical Benefits

1. To improve knowledge about ketogenic diet that can be consumed to prevent further development of cancer cells

2. To add new information for others that can be used as a reference.