IN VITRO INVESTIGATION AND ASSESSMENT OF KNOWLEDGE, ATTITUDE AND PRACTICES AMONG COMMUNITY TOWARDS THE EFFECT OF MONOSACCHARIDES ON CANCER

BY

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ABSTRACT

Definite evidence that the sugar can cause cancer is not yet clearly proven. However, high consumption of sugar has been linked to increase the risk factor of cancer. Overconsumption of sugar will contribute to weight gain and changes in the body system. For instance, the growth hormone would be imbalance which subsequently increased the risk of cancer. The *in vitro* study by using cell lines can be adapted to discover sugars behaviours towards cancer cells. Thus, the knowledge on this association needs to be disseminated to the community in order to prevent or reduce the incidence and the prevalence of cancer cases. The research is done by two different paradigms, laboratory and community-based studies. This laboratory study is sought to identify the pattern of normal and cancer cell lines when treated with different monosaccharides (the simplest form of sugars) at different concentration. In addition, the community-based study, cross sectional aims to assess the knowledge, attitude and practice among the community in Kuantan concerning the effect of monosaccharides on cancer. The former study has been conducted by employing the MTT assay on three different cell lines (normal human gingival fibroblast, skin malignant melanoma and colorectal adenocarcinoma) after being exposed with three types of monosaccharides (glucose, fucose and mannose). The MTT assay is a colorimetric technique used to obtain the percentage of the cell viability. The latter was conducted by disseminating the questionnaire to the community in Kuantan. The frequency, one-way ANOVA and Chi-square were conducted for the statistical analyses. The *p*-value is lower than 0.05 was considered significant. Based on this study, the normal cell line was unable to survive when treated with additional monosaccharides. Otherwise, the cancer cell lines were able to survive when treated with the monosaccharides. The level of attitude showing the high score among the community while the level of knowledge and practice among the community were moderate. The association between sociodemographic data (gender and level of education) showed the significant different with level of knowledge. In conclusion the normal cell line cannot tolerate with the additional monosaccharides. The cancer cells were adapted with the environment that has additional monosaccharides. Meanwhile, the level of knowledge and practice among the community concerning the effects of monosaccharides on cancer need to be enhanced.

خلاصة البحث

لم يتم إثبات أدلة واضحة على السكر قد تسبب السرطان بعد. رغم ذلك، قد ارتبط الاستهلاك المرتفع للسكر بزيادة عامل خطر الإصابة بالسرطان. الاستهلاك المفرط للسكر يؤدي إلى زيادة الوزن والتغيرات في نظام الجسم. على سبيل المثال، تصير الهرمون النمو عدم التوازن بسبب زيادة خطر السرطنة. يمكن تكييف الدراسة المختبرية باستخدام خطوط الخلايا لاكتشاف السلوكيات السكريات تجاه الخلايا السرطانية. ومن ثم يجب نشر المعرفة حول هذه الرابطة على المجتمع من أجل الوقاية من إصابة السرطان وانتشارها. يتم تشغيل البحث من خلال نموذجين مختلفين وهما دراسة مختبرية ودراسة مجتمعية. تهدف هذه الدراسة المختبرية إلى تحديد نمط الخلايا الطبيعية والسرطانية عند معالجتها بمختلف السكريات الأحادية (أبسط أشكال السكريات) بتركيز مختلف. وفضلا عن ذلك، تهدف الدراسة المجتمعية المستعرضة إلى تقييم معرفة وموقف وممارسة المجتمع في كوانتان فيما يتعلق بتأثير السكريات الأحادية على السرطان. قد أجريت الدراسة السابقة من خلال استخدام اختبار MTT على ثلاثة خطوط خلوية مختلفة (الخلايا الليفية البشرية اللثة العادية، والورم الميلانيني الخبيث الجلدي وسرطان الغدة القولون والمستقيم) بعد تتعرض لثلاثة أنواع من السكريات الأحادية (الغلوكوز والفوكوز والمانوز). مقايسة MTT هي تقنية قياس الألوان للحصول على النسبة المئوية لعَيُوشِيَّة الخلية. يضاف إلى ذلك، تم إجراء هذا الأخير بتوزيع الاستبانات على مجتمع كوانتان. قد تم إجراء تحليل التكرار وتحليل التباين الأحادي (One-way ANOVA) واختبار مربع كاي (Chi-square) للتحليلات الإحصائية. تعتبر القيمة الاحتمالية أقل من 0.05 كبيرة. وإسناد إلى هذه الدراسة، لم يستطع الخلايا الطبيعية أن تبقى حيا عند معالجتها بسكريات أحادية إضافية بعد اليوم الأول من الحضانة. خلاف ذلك، الخلايا السرطانية يستطيع أن تبقى وتحيي عند معالجتها بالسكريات الأحادية. وجانب إلى ذلك، كان مستوى الموقف بين المجتمع في الدرجة العالية بينما كان مستوى المعرفة والممارسة معتدلا. والارتباط بين البيانات الاجتماعية الديمغرافية (الجنس ومستوى التعليم) يدل على الاختلاف الكبير في مستوى المعرفة. والخلاصة، لم تتمكن الخلايا الطبيعية تبقى مع السكريات الأحادية الإضافية وهذه الحالة مختلفة للخلايا السرطانية التي تستطيع تكييف مع البيئة التي تحتوي على السكريات الأحادية الإضافية. ومن ناحية أخرى، يجب تعزيز مستوى المعرفة والممارسة بين المجتمع فيما يتعلق بتأثير السكريات الأحادية على السرطان.

APPROVAL PAGE

I certify that I have supervised and read this study and that in my opinion, it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a thesis for the degree of Master in Biobehavioral Health Sciences.

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Assoc. Prof. Dr. Muhammad Lokman Md Isa
Supervisor

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a thesis for the degree of Master in Biobehavioral Health Sciences.

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Dean, Kulliyyah of Nursing

DECLARATION

I hereby declare that this dissertation is the result of my own investigations, except where otherwise stated. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at IIUM or other institutions.

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In the name of Allah, the most Beneficent and the most Merciful.
Peace be upon the beloved Prophet Muhammad S.A.W and his family and companions.

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May this research benefits the entire community and ummah.

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LIST OF ABBREVIATIONS

DNA	Deoxyribonucleic acid
RNA	Ribonucleic acid
MOH	Ministry of Health
HGF	Human gingival fibroblast
PhAMA	Pharmaceutical Association of Malaysia
IGF-I	Insulin like growth factor-1
IGFBP-3	Insulin like growth factor-binding protein-3
FGF2	Fibroblast growth factor-2
ATP	Adenosine triphosphate
ROS	Reactive oxygen species
USA	United States America
DMEM	Dulbecco's Modified Eagle Medium
FBS	Fetal bovine serum
DMSO	Dimethyl sulfoxide
CO2	Carbon dioxide
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide
PBS	Phosphate buffer saline
ANOVA	Analysis of variance
PAGE4	Prostate-associated gene 4 (PAGE4)
CD47	Cluster of differentiation 47
SIRP-α	Signal-regulatory protein-α
NF-kB	Nuclear factor kappa-light-chain-enhancer of activated B cells
FasR–FasL	Fas receptor–Fas ligand
CD44	Cluster of differentiation 44
2-FF	2-fluorofucose
AGEs	Advance glycation end products
HK2	Hexokinase-2
SPSS	Statistical Package for the Social Sciences
KNPGRC	Kulliyyah of Nursing Postgraduate Research Centre
IIUM	International Islamic University Malaysia
IREC	Research Ethics Committee
BMI	Body mass index
MCMC	Malaysian Communications and Multimedia Commission
UV	Ultra violet
Apaf-1	Apoptotic Protease Activating Factor 1
IFN-y,	Interferon gamma
IFNGR1	Interferon Gamma receptor 1
TNF-alpha	Tumor necrosis factor-alpha
COX-2	Cyclooxygenase-2
MBP	Mannose-binding protein
IL-1	Interleukin 1
IL-6	Interleukin 6

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF THE STUDY

Cancer is a devastating group of diseases that affecting a lot of people worldwide. Physiologically, the abnormal cells in the body would cease to grow and develop when the errors or damage occurred. In contrary, in cancerous condition the abnormal cells would not stop from growing and developing. The cancer has the ability to be spread to the other parts of the body which is known as metastasis. For instance, the cancer cells that were originated from the lung could be disseminated to the other organs such as kidney, prostate, breast, colon and etc. The spread of cancer would cause the treatment for cancer become more challenging among the healthcare provider. This is due to the complex and difficulties in order to understand the character and behaviour of the cancer cells.

Basically, the general cause of cancer is due to the gene mutation. Every single cell in the body has nucleus, an organelle that stores the genetic materials called as deoxyribonucleic acid (DNA) except to some cells for example, the matured red blood cells. The DNA also could be found in the mitochondria, an organelle that mainly the place for harvesting energy from the food sources. Instead of DNA, the genetic materials could be ribonucleic acid (RNA). The difference between the latter and former is single helix and double helices of sequence of amino acids respectively. The RNA or DNA is just a coding system, which important in translation of the protein. From the code of the genetic materials, the complex protein will be formed. If the problem occur at the level of genetic materials will subsequently cause the errors during the protein formation. The errors could be due to the mutation of the genetic sequence. The

mutations that could be occurred are as follow; missense, nonsense, insertion, deletion, frameshift, duplication and repeat expansion.

Historically, in 1971 the president of United States of America, Richard Nixon had signed The National Cancer Act 1971 which described as “War on Cancer” ("National Cancer Act of 1971", 2018). This declaration of war on cancer shows that the problem related to cancer is very serious. In Malaysia, the Ministry of Health (MOH) had constructed a strategic plan for cancer control program. This program is one of the initiatives made by ministry to decrease the negative impact of cancer by reducing the morbidity, mortality and to upgrade the quality of life of cancer patients and their families (MOH, 2017).

Sugar is an important source of energy needed by the body for cellular activities. In association with the other factors such as sedentary lifestyle and uncontrolled diet sugar could be one of the reasons why the body mass index increases. The excessive intake of sugar is not good for the body as it may be converted into fat and would subsequently cause overweight and obesity. Fat is very important as it helps to keep producing the hormones and growth factors in the body. Nevertheless, overproduction of these hormones and growth factors will enhance the growth of the cancer cells. Cromie (1999) had reported that high level of well-known growth factors increased the risk of several cancers such colorectal cancer, prostate and breast cancer.

The integration of study between laboratory and community-based study is very important to be conducted. Basically, the laboratory study would be the contributors in understanding certain diseases. Meanwhile, the community-based study could benefit in terms of understanding on how the local environments would giving the impact on the level of knowledge, attitude and practice of the community. Therefore, the

integration between laboratory and community-based study would give positive impact in order to increase the level of understanding on certain diseases.

1.2 STATEMENT OF THE PROBLEM

To date, there is no sufficient evidence reporting that sugar can directly can cause cancer, nonetheless excessive sugar consumption may alter the physiological of the body which indirectly contributed to increase the cancer risk. Commercially, there are varieties of sweetener or simple sugar that has been sold in the market. The consumption of excessive sugar is already well known could cause diabetes. However, the information on the monosaccharides causing cancer is insufficiency. In order to find the treatment for the cancer, the information on the behavior and pattern of the cancer cell growth is very crucial to know. Among the type of monosaccharides available in the market, which one is the most favorable for cancer cell lines? In addition, is there any differences or similarities of cell viability between normal and cancer cell lines? Therefore, the first paradigm of this study attempts to distinguish the cell viability of the normal and cancer cell lines after exposed to different type of monosaccharides.

Previously, Malaysia already launched a lot of campaign on reducing the consumption of sugar in food and drinks. For instance, on the day of 14 January 1998 Malaysia had launched a campaign on awareness the consumption of sugar in Kuala Lumpur ("Hari Ini Dalam Sejarah", 2011). The campaign is very important in order to increase the knowledge of people on the danger of excessive sugar consumption. Among the community of Kuantan, Pahang the level of knowledge, attitude and practice concerning the relationship between sugar and cancer is remain unknown. Perhaps, the people in Kuantan are aware that sugars can cause diabetes. But, do they aware that sugars also can associate to increase the cancer risks? Therefore, an assessment on

knowledge, attitude and practice among the community is very important in order to prevent the increase of cancer statistics by providing the literature concerning this issue.

1.3 PURPOSE OF THE STUDY

This research sought to investigate the behaviour of the normal and cancer cells when treated with different type of monosaccharide at various concentration. The percentage of cell viability the normal and cancer cell lines were obtained in order to appreciate their pattern of living. The information from the laboratory investigation could provide more literature to the body of knowledge concerning the behavior of cancer cells when treated with monosaccharides in comparison with the normal cells. In addition, the other purpose of this study is to conduct an assessment of the level of knowledge, attitude and practice among community especially in Kuantan concerning the association between monosaccharides and cancer. The study focused on the Kuantan residence on their viewpoint on monosaccharides and cancer. The findings of the survey could be used by the healthcare provider in improving the education on health especially in relation to cancer study involving the latest laboratory finding of *in vitro* study. Indeed, the education is powerful for reducing the morbidity and mortality of many diseases.

1.4 RESEARCH OBJECTIVES

The study aimed to achieve the following objectives:

1. To evaluate the viability pattern of human cancer and normal cell lines treated with three different types of monosaccharide derivatives (glucose, mannose and fucose).

2. To assess the viability pattern of human cancer and normal cell lines treated with different concentration of each monosaccharide derivatives (glucose, mannose and fucose).
3. To investigate the level of knowledge, attitude and practice among the Kuantan community concerning the relationship between cancer and monosaccharide derivatives.
4. To identify the association between sociodemographic factors with knowledge, attitude and practice among the Kuantan community concerning the relationship between cancer and monosaccharide derivatives.

1.5 RESEARCH QUESTIONS

1. Which of the monosaccharide derivatives (glucose, mannose and fucose) can affect the viability pattern of human cancer and normal cell lines?
2. Which concentration of each of the monosaccharide derivative (glucose, mannose and fucose) is the most favorable for the cell viability?
3. What is the level of knowledge, attitude and practice among the community concerning the relationship between cancer and sugar?
4. Which of the sociodemographic factors that would have association with the level of knowledge, attitude and practice among the community concerning the relationship between cancer and sugar?

1.6 RESEARCH HYPOTHESES

It could be hypothesized that the monosaccharides could enhance the cancer cell viability. In addition, the level of knowledge, attitude and practice on the relationship between cancer and sugar among the community are low.

1.7 SIGNIFICANCE OF THE STUDY

In this study, some of the monosaccharides are commonly consumed by the people were tested. The test is very essential to see the pattern of the viability of cancer and normal cell lines. Based on the pattern of the cells we could know the sugar that most favorable by the cancer cells. The findings of this study would be helpful for the physician to suggest the cancer patients to reduce or avoid the intake of sugar derivatives that may increase the risk factor of getting cancer. In addition, from the finding of this study, the therapy for cancer also could be designed in the future by incorporating the most favorable monosaccharide with nanoparticles to detect the cancer cells. The survivor of cancer patients have the tendency to experience the cancer for second time. By knowing the possible risk factors, the survived patients could reduce and control the possible food that would increase the cancer risk factors.

The prevention is better than cure. It is well known that cancer is very unpredictable and it could affect anyone at any time. Until now, the prevention of cancer is evolving. This is because cancer is very complex and varieties. This complexity and varieties of cancer are the problem for the healthcare practitioner to prevent the cancer. However, it is well known that there are some factors could increase the risk of getting cancer such excessive sugar intake with minimum exercise. Therefore, at least the prevention of the cancer could be initiated by minimizing the exposure of possible risk factors. In order to minimize the statistic of cancer morbidity and mortality, the government have to educate the citizen on the risk factors that could lead to cancer. It is clearly shown that the information concerning the level of knowledge, attitude and practices among the community is very important. From the information that were obtained from this study, it could help the government to design the strategic plan on how to educate the people of the country. As the education is the best way to minimize

the incidence and the prevalence of certain diseases. Therefore, it is a necessity to optimize the education program for improving and protecting the people's health especially in Malaysia.

1.8 DEFINITION OF TERMS

a) Assessment

Assessment is an action of assessing someone or something.

b) Knowledge

It could be any facts, information, and skills which were acquired from the experience or education.

c) Attitude

Attitude is a way of someone thinking or feeling about something.

d) Practice

It is actual or opposite way of action according to someone thinking or feeling. In which, someone might or might not act according to what their thinking and feeling.

e) Community

A group of people that are sharing similar characteristics such as living the same place or having a particular characteristic in common.

f) Monosaccharide

It is also known simple sugar which is any type of sugar that is no longer can be hydrolyzed into simple sugar.

g) Cancer

Cancer is uncontrolled growth of abnormal cells with the potential to invade and spread to the other parts of body.

1.9 CONCEPTUAL FRAMEWORK

Figure 1.1 illustrates the conceptual framework of the study. There are two paradigms in this study which are laboratory analysis and community-based study. The former paradigm is involving the cell culture technique by using three different type of cell lines including the human gingival fibroblast (HGF), skin malignant melanoma (A375) and colorectal adenocarcinoma (HT29). The cell lines were treated with three types of monosaccharides which are glucose, fucose and mannose at certain concentrations. Meanwhile, the latter paradigm is a community-based study. The study is conducted by applying the cross-sectional study design which it involved the distribution of questionnaire among the Kuantan community. Prior to designing the questionnaire, literature review was conducted. The set of questions is going to be distributed to the community once the content of the questionnaire was validated by the experts

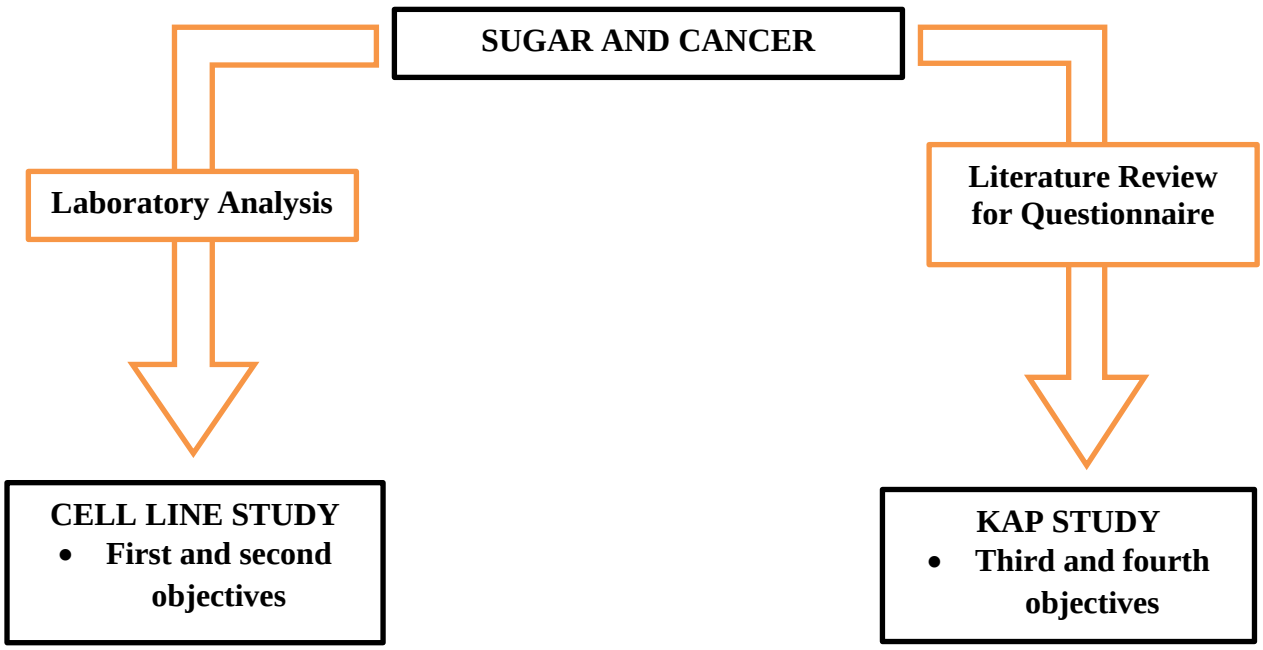

Figure 1.1 The conceptual framework of the study

1.10 CHAPTER SUMMARY

This chapter has presented and discussed the background of the study. It explained why the information on the association between cancer and monosaccharides is vital. The definition of concepts also has been included with numerous citations. Furthermore, the problem statement was discussed, the study was set to discover the pattern of the cell lines when treated with different type of monosaccharides and to assess the level of knowledge, attitude and practice among community. This was followed with the purposes, objectives, research questions, hypothesis and the significance of the study. This chapter also presented the brief definition of terms in this study. Finally, figure 1.1 is the conceptual framework diagram for this study.

CHAPTER TWO

LITERATURE REVIEW

2.1 INTRODUCTION

Since the main concern of this study is to investigate the association between the monosaccharides and cancer. Therefore, the available literatures about the monosaccharides and cancer is essential to be reviewed in this chapter. The review emphasized on the association between the monosaccharides and cancer. In addition, the literatures about the awareness on the sugar consumption were added in this chapter; to discuss on the importance of knowledge, attitude and practice in reducing the risk of getting cancer.

2.2 OVERVIEW OF CANCER

Cancer is a group of diseases which the abnormal cells are developing uncontrollably with unregulated growth. It has the potential to allow the cancer cells to invade and spread to the other parts of body. These cancer cells would infiltrate and cause the normal cells to die. Cancer is a big group of diseases that have many types of cancer. It could be lung, prostate, skin, colorectal cancer and et cetera. The cancer was classified based on the area of the cancer begins to spread and the type of cells. For instance, leukemia is one type of cancer that could cause fatality. Leukemia is a cancer of bone marrow, the place for blood cells production. If the cancer involving the immune system is known as lymphoma and myeloma.

Most of cancer have four stages ("Stages of Cancer", 2018). Knowing the stage of cancer is very important for the physician to decide what treatment need to be given to the patients. At the early or first stage of cancer usually only small cancer or tumor

which within the organ. In addition, it has not spread to the lymph nodes or invade the other organs ("Stages of Cancer", 2018). During the second stage, the tumor is larger than in stage 1, but the cancer has not started to spread into the surrounding tissues. However, sometimes cancer cells have spread into lymph nodes close to the tumor. This depends on the particular type of cancer ("Stages of cancer", 2017). Stage 3 means the cancer become larger which it may start to spread into surrounding tissues and there are cancer cells in the lymph nodes in the area. At the fourth stage the cancer already invaded and spread to the other parts of body ("Stages of cancer", 2017). The process of the cancer cells to spread to the other parts called as metastasis ("Metastatic Cancer", 2017).

2.3 CANCER PREVALENCE

Globally, the cancer becomes the second leading cause of death, about 9.6 million deaths in 2018 ("Cancer", 2018). Based on the Ministry of Health Malaysia (MOH) report in 2018, cancer is the fourth biggest killer in Malaysia. In Malaysia, the common cancers among males are lung cancer, followed by nasopharyngeal or nose cancer. The breast cancer become the most common among the females in Malaysia ("Pharmaceutical Association of Malaysia (PhAMA) - Cancer", 2018). It is about 2 million cases of breast cancer that were reported in 2018 ("Breast cancer statistics", 2019). The level of countries' income is also contributing to the statistics of the death due to cancer. The lower and middle incomes of countries were reported with highest prevalence of death caused by cancer. Approximately seventy percent of deaths occur in low- and middle-income countries ("Cancer", 2018). Malaysia is one of the middle-income countries that might contribute to the statistic of the deaths due to cancer. In which, based on World Bank website had classified the income level of Malaysia as