THE EFFECTIVENESS OF BRAZILIAN SPINACH SUPPLEMENTATION ON HEALTH OUTCOMES AMONG TYPE 2 DIABETES PATIENTS IN HOSPITAL PAKAR UNIVERSITI SAINS MALAYSIA

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by

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LIST OF ABBREVIATIONS

ADA	American Diabetes Association
ADIME	Assessments, Diagnosis, Intervention, Monitoring, And Evaluation
ALP	Alkaline Phosphatase
ALT	Alanine Transaminase
AOAC	Association Of Official Analytical Chemists
ASPEN	American Society for Parenteral and Enteral Nutrition
AST	Aspartate Transaminase
BF	Body Fat
BF%	Body Fat Percentage
BMI	Body Mass Index
BP	Blood Pressure
CHD	Coronary Heart Disease
cm	Centimetres
CPG	Clinical Practical Guidelines
CVDs	Cardiovascular Diseases
CVI	Content Validity Index
DBP	Diastolic Blood Pressure
DHQ	Diet History Questionnaire
DKD	Diabetic Kidney Disease
DM	Diabetes Mellitus
DPP-4	Dipeptidyl Peptidase-4
EDTA	Ethylenediaminetetraacetic Acid
ESRD	End-Stage Renal Disease
FBG	Fasting Blood Glucose
FFA	Free Fatty Acids
FFQ	Food Frequency Questionnaire
FPG	Fasting Plasma Glucose
GDM	Gestational Diabetes Mellitus
GI	Glycemic Index
GLP-1Ras	glucagon-like peptide-1 receptor agonists

HbA1c	Haemoglobin A1c
HLA	Human Leukocyte Antigen
HPLC	High-Performance Liquid Chromatography
HUSM	Hospital Universiti Sains Malaysia
IDF	International Diabetes Federation
IDNT	International Dietetics and Nutrition Terminology
IR	Insulin Resistance
ITT	Intention-To-Treat
JEPeM	USM Human Research Ethics Committee
KPP	*Klinik Pakar Perubatan*
KRK	*Klinik Rawatan Keluarga*
LFT	Liver Function Test
LOCF	Last Observation Carried Forward
MDG	Malaysian Dietary Guidelines
MHC	Major Histocompatibility Complex
MODY	Maturity-Onset Diabetes of the Young
NAFLD	Non-Alcoholic Fatty Liver Disease
NCDs	Non-Communicable Diseases
NCI	National Cancer Institute
NCP	Nutrition Care Process
NHMS	National Health and Morbidity Survey
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIHM	National Institute of Health Malaysia
OGLD	Oral Glucose-Lowering Drug
OGTT	Oral Glucose Tolerance Test
PES	Problem, Etiology, Signs/Symptoms
PG	Plasma Glucose
PP	Per-Protocol
PPG	Postprandial Plasma Glucose
RBC	Red Blood Cell
RBS	Random Blood Sugar
RCT	Randomized Clinical Trial
RFT	Renal Function Test

SBP	Systolic Blood Pressure
SDSCA	Summary Of Diabetes Self-Care Activities
SGLT2	Sodium-Glucose Cotransporter 2
SUs	Sulphonylureas
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
TCA	Transitional Continuing Appointment
UKM	Universiti Kebangsaan Malaysia
USM	Universiti Sains Malaysia
WC	Waist Circumference
WHO	World Health Organization
WHR	Waist-To-Hip Ratio
WHS	World Health Survey
WHtR	Waist-To-Height Ratio

LIST OF APPENDICES

KEBERKESANAN SUPLEMENTASI BAYAM BRAZIL TERHADAP HASIL KESIHATAN DALAM KALANGAN PESAKIT DIABETES JENIS 2 DI HOSPITAL PAKAR UNIVERSITI SAINS MALAYSIA

ABSTRAK

Bayam Brazil ialah sejenis sayuran berdaun hijau yang jarang terdapat secara komersial di Malaysia tetapi dianggap mempunyai potensi manfaat kesihatan untuk individu yang menghidap diabetes mellitus jenis 2 (T2DM). Kajian ini menilai kesan suplemen bayam Brazil terhadap hasil kesihatan pesakit T2DM. Satu kajian terkawal rawak berbutakan tunggal telah dijalankan di Hospital Pakar Universiti Sains Malaysia dari Mac hingga Jun 2023 (12 minggu), melibatkan 53 peserta berumur 30 hingga 65 tahun dengan T2DM. Peserta telah diperuntukkan secara rawak kepada kumpulan kawalan (n = 26) yang menerima kaunseling diet standard atau kumpulan intervensi (n = 27) yang menerima kaunseling diet dan suplemen bayam Brazil (15 g setiap hidangan). Dalam Fasa 1, analisis proksimat bayam Brazil (setiap 100 g) menunjukkan kandungan tenaga (35.83 kcal), karbohidrat (6.20 g), dan lemak (0.06 g) yang rendah, dengan tahap protein (2.62 g) dan serat diet (4.15 g) yang sederhana. Fasa 2 menilai antropometrik (indeks jisim tubuh, lilitan pinggang, peratus lemak badan), biokimia (glukosa darah rawak kapilari [RBS], HbA1c, ujian fungsi hati dan buah pinggang), klinikal (tekanan darah), pengambilan diet, dan tingkah laku penjagaan diri pada peringkat awal, minggu ke-6, dan minggu ke-12. Taburan jantina adalah serupa antara kumpulan (27 lelaki, 26 perempuan), dengan purata umur 52.96 ± 10.07 tahun (kawalan) dan 55.70 ± 9.88 tahun (intervensi). Analisis dalam subjek mendedahkan kesan masa yang ketara terhadap indeks jisim tubuh (p = 0.005), lilitan pinggang (p =

0.006), peratus lemak badan ($p < 0.001$), dan pengambilan serat diet ($p = 0.001$). Analisis antara kumpulan mengenal pasti perbezaan yang ketara dalam RBS kapilari ($p = 0.010$) dan pengambilan diet, termasuk tenaga ($p = 0.006$) dan pengambilan karbohidrat ($p = 0.012$). Tiada perubahan ketara yang diperhatikan dalam HbA1c atau parameter kesihatan lain ($p > 0.05$). Ujian fungsi hati dan buah pinggang mengesahkan keselamatan intervensi. Secara ringkasnya, suplemen bayam Brazil meningkatkan tahap RBS kapilari dan pengambilan makanan dengan ketara tanpa kesan buruk, menunjukkan potensinya sebagai suplemen diet untuk pengurusan T2DM. Kajian berskala besar dan jangka panjang selanjutnya disyorkan untuk mengesahkan keberkesanannya.

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ABSTRACT

Brazilian spinach is a green, leafy vegetable that is rarely commercially available in Malaysia but is considered to have potential health benefits for individuals with type 2 diabetes mellitus (T2DM). The present study evaluated the effects of Brazilian spinach supplementation on health outcomes in patients with T2DM. A single-blind randomised controlled trial was conducted at Hospital Pakar Universiti Sains Malaysia from March to June 2023 (12 weeks), enrolling 53 participants aged 30 to 65 years with T2DM. Participants were randomly allocated to a control group (n = 26) receiving standard dietary counselling or an intervention group (n = 27) receiving both dietary counselling and Brazilian spinach supplementation (15 g per serving). In Phase 1, proximate analysis of Brazilian spinach (per 100 g) indicated low energy (35.83 kcal), carbohydrate (6.20 g), and fat (0.06 g) content, with moderate protein (2.62 g) and dietary fibre (4.15 g) levels. Phase 2 assessed anthropometric (BMI, waist circumference, body fat percentage), biochemical (capillary random blood glucose [RBS], HbA1c, liver and renal function tests), clinical (blood pressure), dietary intake, and self-care behaviours at baseline, week 6, and week 12. Gender distribution was similar between groups (27 males, 26 females), with mean ages of 52.96 ± 10.07 years (control) and 55.70 ± 9.88 years (intervention). Within-subject analysis revealed significant time effects on BMI ($p = 0.005$), waist circumference ($p = 0.006$), body fat percentage ($p < 0.001$), and dietary fibre intake ($p = 0.001$). Between-group analysis identified significant differences in capillary RBS ($p = 0.010$) and dietary intake, including energy ($p = 0.006$) and carbohydrate intake ($p = 0.012$). No significant changes were observed in HbA1c or other health parameters ($p > 0.05$). Liver and renal function tests confirmed the safety of the intervention. In summary, Brazilian spinach supplementation significantly improved capillary RBS levels and dietary intake without adverse effects, indicating its potential as a dietary supplement for T2DM management. Further large-scale and long-term studies are recommended to confirm its efficacy.

CHAPTER 1

INTRODUCTION

1.1 Background of the Study

Type 2 diabetes mellitus (T2DM) is the most common form of diabetes and results from a combination of insulin resistance and impaired insulin secretion by pancreatic β-cells. The global rise in T2DM, particularly in low-income countries and among young adults, poses significant challenges for the diagnosis, prevention, and management of this disease due to its substantial impact on lifespan and quality of life (Izzo et al., 2021). According to Ogurtsova et al. (2022), the International Diabetes Federation (IDF) estimated that 536.6 million people were living with diabetes (diagnosed and undiagnosed) in 2021, and this number is projected to increase by 46% to 783.2 million by 2045. In Malaysia, Harris et al. (2019) reported that 3.6 million adults aged 18 and older had diabetes in 2019, with 49% (3.7 million) of cases remaining undiagnosed. Nationally, the prevalence of diabetes in Malaysia has been reported to range from 7.3% to 23.8% across various studies.

Malaysia ranks as the eighth country with the highest diabetes prevalence in the Western Pacific Region (Nazmi et al., 2023). Data from the National Health and Morbidity Survey (NHMS) 2023 show that diabetes prevalence increased from 11.2% in 2011 to 15.6% in 2023, with 9.7% of individuals aware of their condition and 5.9% unaware. Remali et al. (2019) found that Kelantan recorded the highest number of diabetic patients among Malaysian states in 2011, which may be attributed to local dietary patterns that include sweet, sugar-rich foods. According to the Clinical Practice

Guideline *Management of Diabetes Mellitus* (CPG T2DM, 2020), an HbA1c level ≥6.5% is used as the diagnostic threshold for diabetes in Malaysia, consistent with international recommendations.

Poor glycaemic control often leads to micro- and macrovascular complications such as diabetic nephropathy, retinopathy, neuropathy, stroke, and coronary artery disease. Elevated blood glucose levels adversely affect biochemical markers, increase the risk of coronary heart disease (CHD), and raise mortality among individuals with diabetes. Intensive hyperglycaemia management has demonstrated superior efficacy in decreasing complication rates compared to standard treatment (Awang & Ja'afar, 2020). Therefore, regular monitoring of HbA1c is essential to maintain quality of life, minimise complications, and prevent premature mortality in individuals with T2DM. Despite these concerns, 95% of Malaysian adults do not meet the recommended daily intake of five servings of fruits and vegetables (NIHM, 2019). The Malaysian Dietary Guidelines (MDG, 2020) recommend consuming 3–5 servings of fruits and vegetables each day.

Vegetables are naturally low in fat, sodium, and calories, while being rich in essential nutrients such as vitamins, minerals, protein, fibre, and bioactive compounds, making them important for health promotion (Chen et al., 2018). Insufficient intake of fruits and vegetables (F&V) is a significant modifiable risk factor contributing to the increasing burden of non-communicable diseases (NCDs). Dietary fibre from vegetables reduces the risk of obesity, diabetes, heart disease, stroke, and several cancers (Devirgiliis et al., 2024). Increasing fibre-rich vegetable consumption can help manage body weight by enhancing satiety and reducing body fat. Higher dietary fibre intake has also been associated with improved fat distribution, with normal-weight and overweight individuals typically consuming more fibre than those with obesity (Nour et al., 2018).

Among individuals with T2DM, low-glycaemic-index, non-starchy green leafy vegetables high in fibre have been shown to lower postprandial blood glucose levels and improve overall glycaemic control (Yen et al., 2022). Increased vegetable intake supports better glucose metabolism regardless of diabetes status and offers a simple, effective approach to prevent diabetes progression and reduce vascular complications (Dias & Imai, 2017). Management of T2DM commonly requires pharmacological treatment alongside dietary modifications and weight management, all of which contribute to improved blood pressure (BP) and glycaemic control. Incorporating fruits, vegetables, and whole grains or following dietary patterns such as the Mediterranean or low-glycaemic-index diet can support blood pressure regulation among individuals with diabetes (Filippou et al., 2021). Thus, increasing vegetable consumption to raise dietary fibre intake may enhance overall quality of life in people with T2DM.

However, no studies in Malaysia have examined the potential benefits of Brazilian spinach (*Alternanthera sissoo*) for individuals with diabetes. Given its low consumption among Malaysians, affordability relative to other vegetables, and ease of cultivation, Brazilian spinach may represent a valuable dietary option for diabetes management. Therefore, this study aims to determine the effect of a 12-week Brazilian spinach supplementation on health outcomes among patients with T2DM, particularly in the Kelantan region. It is hypothesised that participants receiving Brazilian spinach will show significant improvements in anthropometric measurements, biochemical markers, clinical indicators, and dietary intake compared with the control group.

1.2 Problem Statement

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder that poses a significant global health challenge, with its prevalence steadily rising in both developed and developing countries, including Malaysia (Lin et al., 2020). The condition, characterized by persistent hyperglycaemia due to insulin resistance and impaired insulin secretion, in which the pancreas does not produce enough insulin or the body cannot utilise it effectively is a defining feature of the disease. This condition leads to long-term complications such as cardiovascular diseases, kidney failure, neuropathy, and retinopathy. The rising incidence of T2DM, particularly in low- and middle-income countries, has placed a heavy burden on healthcare systems, patients, and their families (Ganasegeran et al., 2021). Malaysia, with the highest prevalence of diabetes in the Western Pacific region and among the highest globally, is a clear example of this trend, driven by population growth, ageing, urbanisation, and rising rates of obesity and physical inactivity (Akhtar et al., 2022).

Despite the advancements in pharmacological treatments, many patients continue to struggle to achieve optimal glycaemic control, often due to dietary and lifestyle factors. Diet, particularly fruit and vegetable consumption, plays a crucial role in the management of T2DM (Yen et al., 2022). Fruits and vegetables rich in essential nutrients such as potassium, folate, vitamins, fibre, antioxidants, and phenolic compounds, all of which are vital for disease prevention and maintaining overall health

(Livingstone et al., 2020). Although increased vegetable intake is linked to improved lipid profiles, better glycaemic control, and reduced risk of complications, inadequate vegetable consumption remains a significant concern (Trautwein & McKay, 2020).

Studies consistently show that individuals with T2DM often fail to meet the recommended daily vegetable intake, despite vegetables being rich sources of fibre, vitamins, minerals, and antioxidants essential for glycaemic control and metabolic health (Ahmed et al., 2020). Shu et al. (2017) reported that individuals with T2DM in Selangor, Malaysia, consumed insufficient fruits, vegetables, seafood, legumes, and dairy products. National data similarly indicate low compliance: only 10.2% of men and 10.8% of women in the B40 income group meet the recommended intake of fruits and vegetables daily. Tan et al. (2022) further found that just 2.2% of men and 3.3% of women consumed more than five servings per day, highlighting widespread inadequate dietary practices.

A well-balanced diet with sufficient fruit and vegetable intake, at least two servings of fruit and three servings of vegetables per day, can significantly reduce the risk of diabetes. The unique combination of micronutrients, antioxidants, phytochemicals, and fibre in these foods contributes to lowering the risk of chronic diseases (Trautwein & McKay, 2020). Reflecting this, the revised Malaysian Food Pyramid (2020) places fruits and vegetables at its base, thus encouraging greater daily consumption. The Malaysian Dietary Guidelines (MDG, 2020) recommend a minimum of five servings per day, with any lower intake considered inadequate (Tan et al., 2022).

Insufficient vegetable intake among Malaysian adults contributes to inadequate dietary fibre consumption, which can negatively impact health. Regular consumption of fruits and vegetables is particularly important for managing diet-related chronic diseases such as T2DM, as it helps regulate blood glucose levels, supports weight management, and enhances satiety. Vegetables, in particular, are excellent sources of fibre and offer numerous health benefits (Ahmed et al., 2020). Consistent consumption of high-fibre foods including fruits and vegetables is recommended to help individuals with diabetes control blood sugar and prevent complications (Koponen et al., 2019).

Despite the numerous benefits of a well-balanced diet with sufficient fruit and vegetable intake, many individuals with T2DM continue to consume insufficient vegetables daily. Low dietary compliance, poor awareness, and limited access to appealing and affordable options often contribute to this issue (Chen et al., 2018). Given busy lifestyles and increasing living costs, promoting low-cost and easy-to-grow vegetables is essential to improving dietary habits among T2DM patients. Brazilian spinach (*Alternanthera sissoo*) is a nutrient-dense green vegetable which becoming more popular in Malaysia due to its affordability, availability, and cultural acceptability. Rich in fibre, antioxidants, and bioactive compounds, it may positively influence glucose regulation, dietary balance, and metabolic health (Emmy et al., 2022).

However, scientific evidence on the effectiveness of Brazilian spinach in improving health outcomes among T2DM patients is limited, particularly in comparison with standard dietary counselling. Therefore, there is a need to investigate whether Brazilian spinach supplementation, alongside dietary counselling, can substantially improve health outcomes among individuals with T2DM compared with dietary counselling alone.

1.3 Rationale of the Study

Diabetes mellitus (DM) is among the most severe public health issues that are faced globally due to its increasing prevalence and extensive range of health issues that it creates. Its impact on public health and economic growth throughout the globe is especially negative (Chan et al., 2020). While some countries have seen a decrease in disease incidence, Lin et al. (2020) indicate that the prevalence of diabetes has increased in most developing and developed nations over the last few decades. As reported by Ganasegeran et al. (2020), Malaysia holds the highest diabetes prevalence in the Western Pacific region and ranks among the highest globally. Consequently, a national survey in 2019 revealed that approximately 3.6 million Malaysians aged 18 and older were diagnosed with diabetes, while an additional 3.7 million cases went undetected. By 2025, it is anticipated that 7 million Malaysians aged 18 and older will develop diabetes, leading to a prevalence rate of 31.3%, which poses a significant public health threat (Akhtar et al., 2022).

Vegetables are considered essential components of the staple diet due to their well-known health benefits associated with their nutrient functions and their role as significant sources of dietary fibre (Emmy et al., 2022). According to the American Diabetes Association (ADA), individuals with diabetes should increase their intake of fibre-rich foods such as fruits and vegetables to help reduce their glycaemic index. Therefore, it is important to motivate people with T2DM to incorporate more high-fibre foods into their diets. A recent survey by the National Health and Morbidity Institute (NHMS, 2023) indicates that 95.1% of Malaysian adults fail to consume the recommended five servings of fruits and vegetables each day, despite an overall increase in consumption among the population.

Brazilian spinach (*Alternanthera sissoo*) is gaining recognition in Malaysia as a cost-effective and nutritious vegetable choice due to its widespread commercial cultivation. Its potential to contribute to health management, particularly in the context of diabetes, is a source of hope. The rising demand for it in rural regions and its remarkable nutritional benefits have sparked the interest of scientists and nutritionists (Alam et al., 2022). In addition to being rich in fibre, vitamins, and minerals, Brazilian spinach is known to contain various other beneficial natural compounds. Furthermore, it tends to be less appealing to common garden pests, making it easier to maintain the plant's growth (Mohd Hussain & Amir, 2022).

Nonetheless, Malaysian studies have not uniformly explored the impact of Brazilian spinach on health outcomes, especially in individuals with diabetes. The potential impact of this research is significant, as it could provide valuable insights into the mechanisms that clarify the relationship between the consumption of Brazilian spinach and health management. Brazilian spinach serves as a nutritious vegetable choice that can raise awareness about diabetes. The findings of this research could assist authorities in creating an educational intervention program for these patients. Therefore, this interventional study on the effect of Brazilian spinach on health outcomes in patients with T2DM is essential for ensuring that diabetes patients recognise Brazilian spinach as a valuable source of dietary fibre and functional food components.

1.4 Research Questions

Phase 1

1. What is the value of proximate and dietary fibre of Brazilian spinach (*Alternanthera sissoo*) using the Association of Official Analytical Chemists (AOAC) methods?

Phase 2

2. Is there any significant difference in the effects of Brazilian spinach supplementation on anthropometric measurements (BMI, waist circumference, and body fat percentage) between T2DM patients of the intervention group compared to the control group?
3. Is there any significant difference in the effects of Brazilian spinach supplementation on biochemical profile (capillary random blood sugar (RBS), glycated haemoglobin (HbA1c), liver function test (LFT), and renal function test (RFT)) between T2DM patients of the intervention group compared to the control group?
4. Is there any significant difference in the effects of Brazilian spinach supplementation on clinical measurements (blood pressure) between T2DM patients of the intervention group compared to the control group?
5. Is there any significant difference in the effects of Brazilian spinach supplementation on dietary intake (calories, carbohydrates, protein, fats,

dietary fibre, sugar, and sodium) between T2DM patients of the intervention group compared to the control group?

6. Is there any significant difference in the effects of Brazilian spinach supplementation on the Summary of Diabetes Self-Care Activities (SDSCA) between T2DM patients of the intervention group compared to the control group?

1.5 Research Objective

In relation to the research questions, this section outlines the objectives of this study. There is one general objective and five specific objectives, as outlined below.

1.5.1 General Objective

To determine the effects of 12-week Brazilian spinach on health outcomes among type 2 diabetes (T2DM) patients in Hospital Pakar Universiti Sains Malaysia.

1.5.2 Specific Objectives

This study consists of two phases:

Phase 1

1. To determine the proximate and dietary fibre value of Brazilian spinach (*Alternanthera sissoo*) using the Association of Official Analytical Chemists (AOAC) methods.

Phase 2

1. To compare the effect of 12-week Brazilian spinach supplementation on the anthropometric measurement (BMI, waist circumference, and body fat percentage) between the intervention and control groups of T2DM patients.
2. To compare the effect of 12-week Brazilian spinach supplementation on the biochemical profile (capillary RBS, HbA1c, LFT, and RFT) between the intervention and control groups of T2DM patients.
3. To compare the effect of 12-week Brazilian spinach supplementation on clinical measurements (blood pressure) between the intervention and control groups of T2DM patients.
4. To compare the effect of 12-week Brazilian spinach on dietary intake (calories, carbohydrates, protein, fats, dietary fibre, sugar, and sodium) between the intervention and control groups of T2DM patients.
5. To compare the effect of 12-week Brazilian spinach on the Summary of Diabetes Self-Care Activities (SDSCA) between the intervention and control groups of T2DM patients.

1.6 Research Hypotheses

1. There is a significant difference in the effect of Brazilian spinach supplementation on the anthropometric measurement (BMI, waist circumference, and body fat percentage) between the intervention and control groups of T2DM patients.

2. There is a significant difference in the effect of Brazilian spinach supplementation on the biochemical profile (capillary RBS, HbA1c, LFT, and RFT) between the intervention and control groups of T2DM patients.
3. There is a significant difference in the effect of Brazilian spinach supplementation on clinical measurements (blood pressure) between the intervention and control groups of T2DM patients.
4. There is a significant difference in the effect of Brazilian spinach on dietary intake (calories, carbohydrates, protein, fats, dietary fibre, sugar, and sodium) between the intervention and control groups of T2DM patients.
5. There is a significant difference in the effect of Brazilian spinach on the Summary of Diabetes Self-Care Activities (SDSCA) between the intervention and control groups of T2DM patients.

1.7 Operational Definition

1.7.1 Brazilian Spinach

Brazilian spinach, known scientifically as *Alternanthera sissoo*, is a perennial leafy vegetable with a low growth habit that forms a compact mound reaching up to 30 cm in height, making it suitable for bordering pathways in areas with partial shade. It features mid-green, rounded, crinkly leaves and produces small, white flowers. This green leafy vegetable, commonly consumed during the wet season, has a pleasant flavour when steamed or stir-fried, unlike Aibika or Ceylon spinach, which is often unappealing due to its slimy texture. The growing conditions for this vegetable can range from full sun to partial shade, and it thrives best in subtropical and tropical climates with moderately rich loam soils. It tends to proliferate in the spring or during the rainy season (Fitzsimmons, 2023).

1.7.2 Health Outcomes

The phrase “health outcomes” refers to the impacts on health resulting from a specific treatment plan, intervention, or a series of interventions within the healthcare system (Lee & Leung, 2014). The health outcomes of this study focus on the nutritional status of T2DM patients in terms of anthropometry, biochemical, clinical, and dietary.

1.7.3 Supplementation

Supplementation is taking medications or eating specific foods to enhance one’s health (Wierzejska, 2021). This study’s definition of supplementation is the use of Brazilian spinach as a vegetable supplement to promote better health.

CHAPTER 2

LITERATURE REVIEW

2.1 Diabetes Mellitus (DM)

Diabetes mellitus (DM) is a silent pandemic that affects people worldwide. According to Cole and Florez (2020), the high incidence and impairment rates have caused severe health damage worldwide. DM is a chronic, non-communicable metabolic disease characterised by ongoing hyperglycaemia. It may result from peripheral body resistance to the effects of insulin, decreased insulin production, or both (Sapra, 2023). Chronic hyperglycaemia in people with diabetes can harm several organ systems, worsen other metabolic disorders, and lead to potentially fatal health issues. The most frequent microvascular complications include retinopathy, nephropathy, and neuropathy, while macrovascular complications double or quadruple the risk of cardiovascular disease (Goyal et al., 2023).

DM can exist in a variety of forms: type 1, type 2, gestational diabetes, infant diabetes, maturity-onset diabetes of the young (MODY), and secondary causes resulting from endocrinopathies, steroid exposure, etc. Type 1 diabetes (T1DM) and Type 2 diabetes (T2DM) are the two main types of DM. Impaired insulin production and action are the primary causes of T1DM and T2DM. T1DM typically manifests in children or teenagers, unlike T2DM, which usually affects middle-aged and older individuals with persistent hyperglycaemia due to unhealthy eating and lifestyle choices (Sapra, 2023). According to Cole & Florez (2020), the development of T1DM is caused by a severe deficiency in insulin production and secretion, which is the consequence of a complex interplay between autoimmune mechanisms and genetics. The illness often shows symptoms in the early phases of the patient’s life. Insulin resistance secretion is often elevated in most T2DM patients before the onset of the illness.

According to Sapra (2023), the aetiology, presentation, and treatment plan for T1DM and T2DM differ significantly due to their distinct pathophysiologies. The pancreatic islets of Langerhans contain beta cells, which make insulin, and alpha cells, which secrete glucagon. These are the two main subtypes of endocrine cells. Beta and alpha cells continuously modulate the amount of hormone they produce in response to the glucose environment. Glucose levels go excessively out of balance when there is an imbalance between glucagon and insulin. In people with DM, hyperglycaemia is the end result of insufficient or dysfunctional insulin (insulin resistance) (Goyal et al., 2023). Although genetic predisposition, ageing, and environmental variables undoubtedly play a role, there are strong indications that alterations in lifestyle, such as obesity, poor dietary habits, and urbanisation, are the main drivers of insulin resistance and subsequent β-cell damage. Pregnancy, toxicity, hereditary issues, and pancreatic diseases are additional possible causes of DM (Makwero et al., 2018).

2.2 Prevalence of Diabetes Mellitus (DM)

DM is one of the most serious conditions affecting people’s health worldwide and significantly affects public health and socioeconomic development. Although it declined in certain countries, the prevalence of diabetes has increased in most developing and developed countries in recent decades (Akhtar et al., 2020; Lin et al., 2020). According to the International Diabetes Federation (IDF) (2015), 463 million people globally, or 9.3% of all adults, are expected to have diabetes in 2019. In the absence of successful preventive efforts, Saeedi et al. (2019) anticipate that the number will rise to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045. In addition, 374 million individuals between the ages of 18 and 99 had diabetes in 2017, with 50.1% of cases remaining undiagnosed. As to the findings of Akhtar et al. (2022), prediabetes is anticipated to affect 374 million people globally (7.5%) in 2019 and increase to 8.0% (454 million) by 2030 and 5.48 million (8.6%) by 2045.

In developing countries, the prevalence of diabetes patients is relatively higher. Ganasegeran et al. (2021) report that diabetes is the most common disease in Malaysia and the Western Pacific region, with an annual cost of about 600 million US dollars. During 2011-2019, the prevalence of diabetes increased by 68.3%, i.e., from 11.2% to 18.3%. According to a national survey report, 3.6 million Malaysian adults aged 18 years and older suffered from diabetes in 2019, of whom 3.7 million (or 49%) were undiagnosed (Ganasegeran et al., 2020). According to Harris et al. (2019), since Malaysia's prevalence of diabetes stands at 31.3%, 7 million adults older than 18 years are anticipated to develop diabetes by 2025, representing a serious danger to public health. Published papers indicate that Malaysia has a prevalence of diabetes ranging from 7.3% to 23.8%.

In a study published in 2019, Akhtar et al. found that the pooled prevalence of diabetes was 14.39%, or nearly one in seven Malaysians. These results are consistent with a meta-analysis from another Asian country, Pakistan, which found that 14.62% of people there had diabetes. Yet, compared to its neighbouring countries, such as

Indonesia (6.2%) and Singapore (5.5%), Malaysia has a considerably higher prevalence of diabetes (IDF, 2021). When it came to age groups, the age group between 20 and 29 had the lowest prevalence of diabetes (3.16%), while the age group between 60 and older had the highest prevalence (33.46%). Compared to people in their 20s to 29s, people 60 years of age and older have more than ten times higher. The average age of Malaysians in 2017 was 74.4 years, making them the population with the fastest ageing rate in the world (Akhtar et al., 2022).

2.3 Type 2 Diabetes Mellitus (T2DM)

Regarding medical conditions, diabetes is the most prevalent ailment identified globally. Genetic background is a significant risk factor for both types of DM. According to Rajaei et al. (2019), a thorough investigation of the human genome reveals many loci that carry a DM risk. There is evidence connecting polymorphisms in the human leukocyte antigen (HLA) and major histocompatibility complex (MHC) to a higher risk of T1DM. The relationship between genetics and lifestyle, however, is more complex with T2DM. According to Zheng et al. (2017), the onset of T2DM is more subtly caused by an imbalance between insulin levels and sensitivity, which leads to a functional insulin deficit. Two frequent reasons for insulin resistance include ageing and obesity, while there are many other contributing variables. Compared to T1DM, T2DM appears to have a more solid genetic profile based on a wealth of information. Most people with the condition have at least one parent with T2DM (Zheng et al., 2017).

T2DM is a condition distinguished by insulin resistance and beta-cell dysfunction. Initially, a compensatory boost in insulin synthesis keeps blood glucose levels within the normal range. When the illness develops and alters beta cells, the body's ability to respond to insulin is diminished, leading to insulin resistance. In this situation, insulin is ineffective at maintaining glucose homeostasis and must be compensated for by increased insulin synthesis. Nevertheless, insulin production declines with time, resulting in T2DM (Davies et al., 2018). According to Goyal et al. (2023), most individuals with T2DM are obese or have a higher body fat percentage, usually in the abdomen region. This adipose tissue contributes to insulin resistance through several inflammatory mechanisms, such as dysregulation of adipokines and increased generation of free fatty acids (FFA). T2DM primarily affects those over 45 years old. However, it is becoming more prevalent in children, adolescents, and young adults due to rising rates of obesity, physical inactivity, and energy-dense meals (Goyal et al., 2023).

The increasing global and local prevalence of T2DM poses a major risk to public health. With a doubling in prevalence over the past three decades, diabetes is currently the ninth-largest cause of death globally. 10% of the world's population currently has diabetes, with 90% of those cases being T2DM (Zheng et al., 2017). In the Western Pacific Region, the prevalence of diabetes is the eighth-largest in Malaysia. According to the National Morbidity Health Survey, Kelantan diabetes prevalence increased from 11.3% in 2015 to 19.5% in 2019. Uncontrolled diabetes that results from poor glycaemic control is responsible for many problems affecting persons with DM. Omar et al. (2023) found that after ten years of treatment, adult T2DM patients in all of Kelantan experienced improvements in their ability to control their diabetes. However, there is still room for improvement because glycaemic management is an important metric for preventing issues.

According to Davies et al. (2018), diabetes can be identified by measuring plasma glucose concentration (fasting or 2-hour plasma glucose) or by utilising the haemoglobin A1C (HbA1c) criteria. Testing for HbA1c and fasting glucose levels can help in the early diagnosis of T2DM. An oral glucose tolerance test (OGTT) and fasting glucose levels can be measured using a glucose tolerance test if the results are unclear. Following an eight-hour overnight fast, a blood sample is taken. According to the CPG T2DM (2020), the diagnosis is consistent with a fasting plasma glucose (FPG) level greater than 7.0 mm/L. The plasma glucose (PG) level is measured both before and two hours after ingesting 75 g of glucose in this test. Diabetes is diagnosed if the PG level from the 2-hour sample is more than 11.1 mmol/L. Despite being a standard test, it is more costly and inconvenient than FPG and has significant variability issues (Davies et al., 2018).

Diabetes is diagnosed in people whose HbA1c levels exceed 6.5% (45 mmol/mol) (CPG T2DM, 2020). HbA1c is a fast, simple, standardised, and uncomplicated test with minimal variation caused by pre-analytical variables. It is not significantly affected by stress or acute sickness (Goyal et al., 2023). The global nutrition transition, which is a shift in the consumption of high energy-density but low-nutrient food (typically high in sugar and saturated fats, also referred to as the Western pattern diet), and urbanisation and lifestyle changes such as sedentary behaviour and less physically demanding work are all contributing factors towards the rise in incidence in developing countries. The main goal of managing diabetes is to avoid long-term issues. One of the most important strategies for achieving this goal is to maintain and improve glucose control over time. Unfortunately, due to the progressive nature of the disease, this is a challenging task that requires early treatment optimisation, virtually always involving insulin therapy (Davies et al., 2018).

2.4 Diabetes Mellitus Treatments

With diet and exercise alone, some T2DM patients can reach their desired blood sugar levels, but many also require insulin therapy or diabetes medications. Several variables, such as blood sugar levels and other medical issues, influence the choice of the most effective medications (Dwivedi & Pandey, 2020). Preventing microvascular and macrovascular consequences in diabetes requires optimal glycaemic management. It takes a mix of pharmaceutical treatment and lifestyle modifications to establish and maintain optimal metabolic control in diabetes. The risk of macrovascular and microvascular complications is considerably reduced when the HbA1c level is brought close to normal (Roglic & Norris, 2018).

Currently, T2DM can be treated with a variety of injectable and oral medications. Treatment strategies that aim to slow the onset or progression of diabetic complications have a strong emphasis on maintaining optimal glycaemic control. The first line of treatment should be lifestyle modifications. Additionally, although lifestyle modifications are helpful, this is a problem for many patients (Marín-Peñalver et al., 2016). Strategies for reducing blood sugar should reduce the risk of hypoglycaemia, which can impair quality of life, adherence to treatment, and patient satisfaction

(Roglic & Norris, 2018). Practice recommendations advocated a patient-centred approach to selecting oral glucose-lowering drugs (OGLDs) in people with T2DM.

When used as directed, OGLDs can help reduce T2DM symptoms. Unfortunately, a large number of patients who need these medications do not follow their prescribed course of action (Farhat et al., 2019). In order to treat diabetes, doctors should be knowledgeable about the various kinds of drugs currently available and choose the ones that are safe, effective, and easier for patients to tolerate (Marín-Peñalver et al., 2016). In many clinical trials that assessed new OGLDs, metformin served as the basis therapy and is frequently the first-line treatment for T2DM (Amod, 2020). If metformin is not tolerated or glycaemic control is not achieved, alternative OGLDs such as sodium-glucose cotransporter 2 (SGLT2) inhibitors, glucagon-like peptide-1 receptor agonists (GLP-1RAs), dipeptidyl peptidase-4 (DPP-4) inhibitors, sulphonylureas (SUs), and thiazolidinediones may be considered, taking into account the patient's risk of hypoglycaemia or cardiorenal disease (ADA, 2022; CPG of T2DM, 2020).

The ability of Asian individuals with T2DM to overcome insulin resistance was lower than that of white populations (Yabe & Seino, 2016). Accordingly, one common therapeutic approach for Asian patients with T2DM is to increase insulin secretion by the use of insulin secretagogues like SUs (Seino et al., 2017). In conclusion, OGLDs were used to treat most T2DM patients in Asia, with SUs being used to treat about 60% of patients, frequently in conjunction with metformin. SUs (including gliclazide) is a crucial therapy choice for individuals with T2DM due to their good glycaemic control, safety qualities, and affordability (Lim et al., 2022).

Meanwhile, some T2DM patients require insulin therapy. Nowadays, due to its advantages, insulin therapy is frequently administered earlier than in the past, when it was only used as a last resort. One potential side effect of insulin is hypoglycaemia, or low blood sugar (Dwivedi & Pandey, 2020).

2.5 Nutritional Assessments

A nutritional assessment is a comprehensive, systematic evaluation of a patient's nutritional status carried out by medical professionals working together to diagnose malnutrition, find underlying conditions, and develop an intervention plan. The assessment of an individual's nutritional status is necessary to ascertain if the individual has an underlying ailment that is causing the nutritional imbalance or whether the individual is at risk of developing a pathological disease as a result of the imbalance (Reber et al., 2019). For dietary management to be implemented early and successfully, nutritional assessment should be straightforward, efficient, adaptable, and repeatable. Healthy people have different dietary needs depending on their age, sex, and degree of physical activity. As a result, dietary recommendations differ depending on demographic group (Kesari, 2023).

It is crucial to realise that there is no one ideal test for determining nutritional status while doing nutritional assessments. It is advised to gather data methodically, and nutritional status should be evaluated using the complete set of data gathered. As defined by the American Society for Parenteral and Enteral Nutrition (ASPEN), a comprehensive nutritional assessment includes anthropometric measurements, diagnostic testing, dietary assessments, and a comprehensive clinical examination that involves a history and physical examination (Mueller et al., 2011). It is essential to comprehend the distinction between nutritional screening and a thorough nutrition assessment. The purpose of nutritional screening is to identify those who are at risk of malnutrition as early as possible. In contrast, patients who have already been identified as being at nutritional risk undergo a thorough nutritional assessment to determine their present nutritional status (Reber et al., 2019). Kesari (2023) asserts that nutritional assessment enables medical professionals to methodically assess their patients' total nutritional state, detect malnutrition, pinpoint underlying conditions that exacerbate malnourishment, and provide the required treatments.

However, the majority of chronic illnesses are associated with malnutrition, particularly in relation to protein, which is a strong predictor of higher mortality, unfavourable evolution, and prolonged or recurrent hospitalisations. According to Kesari (2023), the main objectives should be to provide patients with chronic illnesses with the proper nutritional treatment through nutritional means such as Medical Nutrition Therapy (MNT) and to place an emphasis on risk detection and quantification as well as its subclinical manifestations. It is commonly known that the nutritional condition of individuals with diabetes is influenced by their eating habits, degree of physical activity, and socioeconomic situation. Better nutritional and clinical results for diabetic individuals require socioeconomic support, nutrition education, and exercise regimens. Patients with low incomes and educational levels may not have access to dietary expertise, which could negatively impact their nutritional status and overall health. Dietary practices and food types affect blood pressure, lipid profiles, and blood glucose levels. Thus, poor nutrition raises the risk of chronic diseases in addition to DM (Bakr, 2015).

For individuals with particular underlying disorders or in specific population groups, additional diagnostic testing or clinical examinations can be necessary. Patients who are nutritionally at risk should undergo a more thorough nutritional evaluation in order to pinpoint and quantify certain dietary issues. Medical history, past and present food consumption (including energy and protein balance), physical examination, anthropometric measurements, functional and mental assessment, quality of life, medications, and lab results are among the subjective and objective components of this assessment (Kesari, 2023). To preserve and enhance patients' nutritional status, interdisciplinary approaches should be used in the development and implementation of nutritional care programmes (Reber et al., 2019).

2.5.1 Anthropometry

The chance of developing chronic conditions like cardiovascular disease, hypertension, and T2DM is increased by abdominal obesity. Numerous risk factors, such as urbanisation, economic growth, population ageing, and obesity brought on by sedentary lifestyles and overeating, have been connected to the higher incidence of T2DM (Mozaffarian, 2016). When visceral fat builds up excessively, endocrine function becomes unbalanced, and pro-inflammatory substances like interleukin-6 (IL-6) are released. This can lead to insulin resistance and T2DM (Lv et al., 2016). According to Han et al. (2019), these substances negatively impact endothelial cells, increasing insulin resistance and the risk of diabetes and dyslipidaemia. Fatty acids and other chemicals produced by the fat in the abdominal organs encourage the blood to release inflammatory chemicals, which prevents the liver from metabolising insulin