THE CHANGES IN GLYCEMIC CONTROL AND CARDIOVASCULAR RISKS AMONG TYPE 2 DIABETES MELLITUS PATIENTS IN KELANTAN ENHANCED PRIMARY HEALTHCARE CLINICS PRE AND POST-COVID-19 PANDEMIC

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by

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LIST OF SYMBOLS

>	More than
<	Less than
=	Equal to
%	Percentage
δ	δ a difference in population means
σ	standard deviation of difference in the response of matched pairs
n	number of patient's data require
P_0	proportion of uncontrolled glycemia among unexposed group from the previous study
P_1	estimated proportion of uncontrolled glycemia among exposed group from the previous study
m	ratio unexposed/ exposed

LIST OF ABBREVIATIONS

AACE   American Association of Clinical Endocrinologists

ADA   American Diabetes Association

Adj. OR   Adjusted Odd Ratio

BMI   Body Mass Index

CAD   Coronary Artery Disease

CCBMTAC   Cardiovascular Care Bundle Medication Therapy Adherence Clinic

CHC   Community Health Coordinator

CHD   Coronary Heart Disease

CI   Confidence Interval

CMCO   Conditional Movement Control Order

CRF   Case Report Form

CV   Cardiovascular

CVA   Cerebrovascular accident

CVD   Cardiovascular disease

DALYs   Disability-adjusted life years

DM   Diabetes Mellitus

EMCO   Enhanced Movement Control Order

EnPHC   Enhanced Primary Healthcare

FPG   Fasting Plasma Glucose

JNC   Joint National Committee

T2DM   Type 2 Diabetes Mellitus

HbA1c   Glycosylated hemoglobin level

HDL-C   high density lipoprotein cholesterol

HF   Heart Failure

IGT   Impaired glucose tolerance

LDL-C   Low density lipoprotein cholesterol

MCO   Movement Control Order

MI   Myocardial ischemia

MOH   Ministry of Health

NCDs   Non communicable diseases

NDR   National Diabetes Registry

NHMS	National Health Morbidity Survey
NSC	National Safety Council
OGT	Oral glucose tolerance
OR	Odds Ratio
PAD	Peripheral artery disease
RMCO	Recovery Movement Control Order
ROC	Receiver Operating Characteristic
SPSS	Statistical Package for Social Sciences
SD	Standard Deviation
TC	Total cholesterol
TG	Trigliserida
T2DM	Type 2 Diabetes Mellitus
WHO	World Health Organisation

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PERUBAHAN KAWALAN PARAS GULA (GLISEMIK) DAN RISIKO KARDIOVASKULAR DI KALANGAN PESAKIT DIABETES MELITUS DI KLINIK ENHANCED PRIMARY HEALTHCARE NEGERI KELANTAN SEBELUM DAN SELEPAS PANDEMIK COVID-19

ABSTRAK

Latar belakang: Diabetes Melitus jenis dua merupakan isu penting kesihatan awam yang kini ditahap yang membimbangkan dan perlu diberi perhatian. Pesakit diabetes mempunyai risiko dua hingga tiga kali lebih tinggi untuk menghidap penyakit kardiovaskular dan kematian pramatang berbanding bukan pesakit diabetes. Pandemik COVID-19 telah memberi kesan kepada gaya hidup dan akses kepada penjagaan kesihatan di kalangan pesakit yang memperburukkan lagi situasi yang sedia mencabar ini.

Objektif: Kajian ini bertujuan untuk melihat perubahan kawalan paras gula (glisemik) dan risiko kardiovaskular sebelum dan selepas pandemik COVID-19 serta faktor-faktor yang berkaitan dengan paras gula yang tidak terkawal selepas pandemik di kalangan pesakit Diabetes Melitus jenis dua di klinik Enhanced Primary Healthcare negeri Kelantan.

Metodologi: Ini adalah kajian secara hirisan lintang data sekunder, yang dijalankan dari 14 Mac 2023 hingga Jun 2023. Dua ratus lima puluh data pesakit Diabetes Melitus jenis 2 diperoleh daripada rekod perubatan pesakit. Analisis deskriptif dan regresi logistik berganda telah dijalankan menggunakan IBM SPSS statistik versi 27.

Keputusan: Purata umur pesakit SD adalah 64.7 (10.40) tahun. Kebanyakan pesakit adalah berbangsa Melayu [236 (94.4%)], perempuan [187 (74.8%)], berkahwin [149 (59.6%)], tidak bekerja iaitu suri rumah [129 (66.2%)], dan [79 (47.6%)] pesakit mempunyai pendidikan menengah, diikuti pendidikan rendah [50 (30.1%)]. Sebanyak 95 peratus pesakit mempunyai komorbid yang mana hipertensi [215 (86.0%)] adalah yang paling tinggi diikuti dengan hiperlipidemia [203 (81.2%)]. Nefropati diabetes [72 (28.8%)] adalah komplikasi diabetes yang paling tinggi diikuti dengan retinopati diabetes [40 (16%)]. Terdapat 182 (72.8%) pesakit dengan kadar paras gula tidak terkawal selepas pandemik COVID-19. Pesakit dengan kadar paras gula tidak terkawal sebelum pandemik COVID-19 mempunyai 16 kali ganda risiko untuk kadar paras gula tidak terkawal selepas pandemik COVID-19 (16.03 (8.11, 31.70), nilai p <0.001). Pesakit dengan peningkatan 1 mmol/l kadar kolesterol total sebelum pandemik mempunyai 1.36 kali ganda risiko untuk memiliki kadar paras gula tidak terkawal selepas pandemik (95% CI: 1.020 hingga 1.806, nilai p <0.05) apabila diselaraskan dengan kadar paras gula tidak terkawal sebelum pandemik COVID-19.

Kesimpulan: Langkah-langkah kawalan pandemik tidak memberi kesan kepada kawalan kadar paras gula dan risiko kardiovaskular yang lain. Faktor individu dalam pengurusan kendiri amat penting untuk memastikan kawalan kadar paras gula yang baik berterusan walaupun terdapat perubahan dalam perkhidmatan penjagaan kesihatan disebabkan oleh pandemik. Pemerkasaan *Chronic Care Model* (CCM) untuk pengurusan penyakit kronik dan teleperubatan merupakan alternatif yang baik bagi pemantauan pesakit, pendidikan kesihatan, konsultasi, dan sokongan psikososial terutamanya dalam situasi pandemik atau bencana.

KATA KUNCI:

Diabetes Melitus jenis dua, COVID-19, *Enhanced Primary Health Care*, faktor berkaitan

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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is a significant health concern and has reached alarming levels. Diabetes patients are two to three times more likely to develop cardiovascular disease and die prematurely than non-diabetics. COVID-19 pandemic has affected lifestyle and healthcare access to patient and exacerbated this challenging situation.

Objective: To study the changes in glycemic control and cardiovascular risk pre and post-pandemic COVID-19 and associated factors of uncontrolled post-pandemic glycemic status among T2DM patients at Kelantan EnPHC clinics.

Methodology: This was a cross-sectional secondary data review, conducted from 14 March 2023 till June 2023. Two hundred and fifty data of Type 2 Diabetes Mellitus patients were acquired from patients' medical records. Descriptive and multiple logistic regression analysis were performed using IBM SPSS Statistics version 27 software.

Result: The mean age was 64.7 (10.40). The majority of patients were Malay [236 (94.4 %)], female [187 (74.8%)], married [149 (59.6%)], unemployed which is housewives [129 (66.2%)] and [79 (47.6%)] patients received secondary education

followed by primary education [50 (30.1%)]. Ninety-five percent of the patients have underlying comorbidities and the highest comorbidities were hypertension [215 (86.0%)] and hyperlipidemia [203 (81.2%)]. Nephropathy [72(28.8%)] was the highest diabetic complication followed by retinopathy [40 (16%)]. There were 182 (72.8%) patients with uncontrolled glycemia post-pandemic COVID-19 respectively. Patient with uncontrolled glycemia pre-pandemic COVID-19 has 16.03 times the odds to have uncontrolled glycemia post-pandemic COVID-19 compared to patient with controlled glycemia pre-pandemic when adjusted for total cholesterol level pre-pandemic COVID-19 (16.03 (8.11, 31.70), p-value <0.001). Patient with an increase in 1 mmol/l of total cholesterol level pre-pandemic has 1.36 times the odds to have uncontrolled glycemia post-pandemic (95% CI: 1.020 to 1.806, p-value <0.05) when adjusted for uncontrol glycemic pre-pandemic COVID-19.

Conclusion: The pandemic restrictive measures do not affect glycemic control as well as other cardiovascular risks. Individual patient factor on self-management is important to ensure the continuation of good glycemic control despite changes in healthcare services due to the pandemic. Enhancing the implementation of a chronic care model (CCM) for chronic disease management and telemedicine is a good alternative for patient monitoring, health education, consultation, and psychosocial support especially during a pandemic or disaster situation.

KEYWORDS:

Type 2 Diabetes Mellitus, COVID-19, Enhanced Primary Health Care, associated factors

CHAPTER 1

INTRODUCTION

1.1   Type II Diabetes mellitus (T2DM)

Diabetes mellitus is a chronic metabolic condition marked by persistently elevated blood glucose levels (hyperglycemia). It can be caused by inadequate insulin secretion or decreased sensitivity to the effects of insulin on carbohydrate, lipid, and protein metabolism (MOH, 2020b; Dianna J Magliano (Co-chair), 2021). Type II Diabetes Mellitus (T2DM) often develops later in life and is characterized by abnormalities in metabolic balance. The complex nature of T2DM, which affects the pancreas and metabolic organs via multiple pathophysiological pathways, makes effective treatment difficult to accomplish. Rapid globalization, an aging population, and sedentary lifestyles which is lack of physical activity in addition to unhealthy diets contributed to the worldwide development of this disease. More than 90% of worldwide cases of diabetes are T2DM. The 2019 National Health Morbidity Survey (NHMS) reported that prevalence of diagnosed diabetes in Malaysia increased from 8.3% (95% CI: 7.8, 8.8) in 2015 to 9.4% (95% CI: 8.66, 10.20) in 2019, equivalent to approximately 2 million individuals. While the prevalence of undiagnosed diabetes (defined as increased fasting plasma glucose of ≥ 7.0 mmol/L) among adults aged more than 18 years in the NHMS 2015 was decrease from 9.2% (95% CI: 8.5, 9.9) to 8.9% (95% CI: 7.96, 9.93) in 2019 (NIH, 2015; NIH, 2019a; MOH, 2020a). Nephropathy, retinopathy and neuropathy are all microvascular complications that are strongly linked to T2DM (Syed Soffian *et al.*, 2019; MOH, 2020c; Harbuwono *et al.*, 2022).

Diabetes patients are two to three times more likely to develop cardiovascular disease and die prematurely than non-diabetics (NIH, 2019a; Stoian, 2021).

1.2   COVID-19

The emergence of a new coronavirus, COVID-19 or SARS-CoV-2, was initially reported in Wuhan, China, in December 2019. The high transmission rate and potential fatality of this virus has raised global concerns. This disease can give rise to symptoms that range from moderate flu-like manifestations to severe pneumonia, respiratory failure, and fatality (NIH, 2020b). Commonly observed symptoms of COVID-19 include fever, runny nose, dry cough, fatigue, loss of taste or smell, headache, diarrhoea, sore throat, and vomiting. The average duration of the incubation period is 5 to 6 days, with the potential to extend of up to 14 days. The primary modes of transmission for COVID-19 are via respiratory droplets and contact with mucosal membranes in the oral, nasal, and ocular regions. SARS-CoV-2 can survive on different surfaces for several days. As the manifestation of symptoms becomes apparent, the amount of virus present in the body decreases, leading to a reduction in the level of contagiousness. Notwithstanding, individuals who exhibit mild or no symptoms may still harbour a substantial amount of virus in their upper respiratory tracts. COVID-19 was declared a Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO) in January 2020, and it was later declared a pandemic on March 11, 2020. (Azarpazhooh *et al.*, 2020; Fronteira *et al.*, 2021).

On January 23, 2020, lockdown was initially enforced in Wuhan, which was the epicentre of the epidemic in China. Numerous nations impacted by the COVID-19 outbreak were advised to execute containment and mitigation strategies in accordance with the guidelines provided by the WHO to reduce the transmission of the disease. These measures involve early detection, isolation, and treatment of infected individuals, along with particular tracing and screening of their contacts. Malaysia has enacted a nationwide lockdown through the Movement Control Order (MCO) on March 18, 2020 as an effort to mitigate the disease's spread, lower the virus's transmission rate, and lessen its effects as the second wave of COVID-19 saw an exponential rise in the daily number of positive instances. The National Safety Council (NSC) of Malaysia, which operates under the purview of the Prime Minister's Department, was mobilised through the National Security Council Act 2016 (Act 776) to coordinate the governmental and non-governmental system at a national scale. The National Security Council (NSC) has established stringent standard operating procedures (SOPs) that required Malaysians to primarily remain indoors and practise social distancing measures. Numerous limitations have been implemented, such as the practise of social distancing, the closure of offices, schools, universities, and nonessential enterprises, as well as the prohibition of public gatherings, religious assemblies, and interstate and international travel. In order to contain the spread of COVID-19, an Enhanced Movement Control Order (EMCO) will be enforced in regions where there is a high prevalence of positive cases (i.e., 40 or more cases). This measure entails a complete lockdown of the affected areas. The Malaysian government subsequently impose a less restrictive measure, the Conditional Movement Control Order (CMCO) and the Recovery Movement Control Order (RMCO) in response to

the decreasing trend of COVID-19 cases (Al-Tawfiq *et al.*, 2020; Aziz *et al.*, 2020; NIH, 2020b; NIH, 2020a; Ang *et al.*, 2021).

Numerous modifications have been implemented in healthcare facilities with the aim of minimising COVID-19 exposure and safeguarding both patients and healthcare personnel. The healthcare facility has implemented a reinforced staggered appointment system, wherein non-essential or follow-up appointments for stable patients are temporarily deferred, and elective procedures are either rescheduled or reduced following a clinical evaluation by the attending physician. The decisions were made in response to a shortage of healthcare personnel resulting from staff reallocation to address the escalating need for COVID-19 patient care (Al-Tawfiq *et al.*, 2020; Amu *et al.*, 2020; Chang *et al.*, 2021; Zhang *et al.*, 2022).

1.3   The Enhanced Primary Healthcare (EnPHC)

"Enhanced Primary Health Care" (EnPHC) was piloted in July 2021 in Johor and Selangor, involving twenty (20) health clinics. Subsequently, the initiative was extended to Seremban in the year 2019 and to five (5) healthcare clinics in Kelantan in March of 2020. The EnPHC adopts a proactive approach that prioritises early disease prevention, targeted non-communicable disease management, surveillance, and continuous patient monitoring. It is aimed to minimize the impact of non-communicable diseases (NCDs) and prioritising the enhancement of service provision at the primary healthcare level.

The EnPHC programs experienced an interruption during the initial stages of the COVID-19 pandemic due to mobilization of not only human resources, but other materials and financial resources to control the pandemic. The pandemic posed

difficulty in accessing healthcare due to limited resources and restrictive measures which follows the escalating number of cases and fatalities (Al-Tawfiq *et al.*, 2020; Perialathan *et al.*, 2021).

1.4   Problem statement

The COVID-19 pandemic had posed challenges to the healthcare system. EnPHC which focus on NCD management should be functioning as usual and should not be neglected despite the pandemic situation. Management of chronic diseases, especially serious complication must not only be maintained efficiently but also in a safe way (Luna and Luyckx, 2020). However, as more resources are mobilized to combat the pandemic, the non-COVID health services including NCDs may be compromised. The combined effects of the COVID-19 pandemic and restrictive measures have created even more significant barriers and challenges to access primary care services. Fear of visiting clinics due to the perceived higher risk of contracting SARS-CoV-2, limited mobility during lockdown periods, and reduced availability of non-urgent and routine clinic visits, including outright cancellation of such programmes were among barriers to healthcare access (Al-Tawfiq *et al.*, 2020; Amu *et al.*, 2020). Public health measures implemented to prevent the spread of the virus such as social distancing, and restrictions in activities had also led to major changes in lifestyle where people become more sedentary which may add on risk of NCDs (Ang *et al.*, 2021; Bennett *et al.*, 2021; Ojo *et al.*, 2022). More than 60% of nations assessed by WHO in May 2020 reported disruptions in NCD services, whether partial or complete (Amu *et al.*, 2020; WHO, 2020; Chang *et al.*, 2021). The top 10 causes of death statistics in Malaysia by DOSM 2022 may reflect similar disruption of chronic disease management where seven out

of the top 10 causes of death which account for 28.3% are NCDs. Cardiovascular diseases (CVD) which include ischemic heart disease, cerebrovascular accident and hypertensive diseases account for the majority of it (21.9%), whereby diabetes as one of risk factors for CVD accounts to 1.8% of the top leading cause of death in Malaysia (DOSM,2022).

1.5 Rationale of the study

The COVID-19 pandemic had placed our healthcare system into a challenging situation where services had to be reorganized and given priority to control the spread of the deadly infectious disease epidemic. The Malaysian MOH had been maneuvering healthcare services to minimize these effects. This study looked at the changes of glycemic control and other CV risk factors among T2DM patients before the pandemic and during the transition to endemic phase. These findings may provide evidence on the impact of pandemic control onto diabetes management. This may also reflect the magnitude of disruption of NCDs management in general or as one of the information that support the effort of the MOH in balancing the effort of pandemic control with other health services.

1.6 Research Questions

1. Does glycemic control of T2DM patients in Kelantan worsen at post-pandemic COVID-19?

2. Do cardiovascular risks among T2DM patients in Kelantan increase at post-pandemic COVID-19?

1.7   Objectives

1.7.1   General Objectives

To study the changes in glycemic control and cardiovascular risk pre and post-pandemic COVID-19 and associated factors of uncontrolled post-pandemic glycemic status among T2DM patients at Kelantan EnPHC clinics

1.7.2   Specific Objectives

1. To compare mean HbA1c and cardiovascular risk factors (body weight, blood pressure, lipid profile) pre and post- pandemic among T2DM patients at Kelantan EnPHC clinics
2. To determine the associated factors of uncontrolled post-pandemic glycemic status among T2DM patients at Kelantan EnPHC clinics

1.8   Research hypothesis

1. There are significant changes in mean HbA1c between pre and post-pandemic in T2DM patients at Kelantan EnPHC clinic.
2. Sociodemographic and clinical characteristic factors are significantly associated with uncontrolled post-pandemic glycemia among T2DM patients at Kelantan EnPHC clinic.

CHAPTER 2

LITERATURE REVIEW

2.1   Non-communicable diseases (NCDs)

Non-communicable diseases (NCDs) are characterised by their long duration and gradual progression. NCDs impose a significant socio-economic burden as a result of raised morbidity, disability, and premature mortality. The prevalence of NCDs has escalated at a rapid pace in low- and middle-income countries (LMICs), such as Malaysia, in recent times, as a result of urbanisation, westernisation, and unhealthy lifestyle (Ekoru *et al.*, 2019; Owopetu *et al.*, 2021). Seventy three percent of deaths and 62% of disability-adjusted life years (DALYs) in 2017 were attributable to NCDs which cardiovascular disease (CVD) was responsible for 32% of deaths and 15% of DALYs among these conditions. Central Europe, Eastern Europe, and Central Asia had the highest number of DALYs due to NCDs which was 29870.3 per 100,000 population followed by the high-income region which was 23778.2 per 100,000 population. Death rates from NCDs followed a similar trend. (Azarpazhooh *et al.*, 2020). The etiology of most NCDs can be attributed to four specific behavioral patterns, namely tobacco use, a sedentary lifestyle, unhealthy diet, and excessive alcohol intake. These behaviours lead to four distinct metabolic and physiological changes namely hypertension, overweight/obesity, hyperglycemia, and hypercholesterolemia. Non-modifiable risk factors for NCDs include age, gender, ethnicity, and family history (genetic), whereas modifiable risk factors include an unhealthy diet, physical inactivity, tobacco use, and smoking. The adoption of a

healthy lifestyle, which includes a healthy diet, increased physical activity, cessation of tobacco use, and effective stress management, has been shown to reduce the likelihood of chronic disease development and enhance overall quality of life (MOH, 2017; MOH, 2020b).

In 2019, 1.7 million Malaysians, which accounts for 8.1% of the population, were at significant risk for non-communicable diseases due to diabetes, hypertension, and high cholesterol. In Malaysia, 30.4% of adults were found to be overweight and 19.7% were classified as obese, making up a total of 50.1% of the adult population. Between 2011 and 2015, there was an increase in the prevalence of abdominal obesity among adults, with 52.6% being affected which was increasing trend compared to 2011 and 2015 (NIH, 2019b). According to data from 2019, approximately 25.1% of adults were physically inactive. Approximately one-third of individuals living in urban areas lead a sedentary lifestyle, while a staggering 95% of adults in Malaysia fail to consume the recommended daily intake of fruits and vegetables. Long-term care for chronic illness involves regular clinic visits, access to medication, proper medication use, lifestyle adjustments, and management of any complications that may arise (NIH, 2019a; MOH, 2020a). Improving continuity of care can lead to various benefits such as increased patient satisfaction, better adherence to prescribed medications and health-promoting behaviors, fewer hospitalizations, and even reduced mortality rates (Lau and McAlister, 2021).

Pre-pandemic statistics in Malaysia reported that NCDs contribute to 71% of premature deaths (Ministry of Health Malaysia, 2020, Chandran et al., 2021, WHO, 2021). Report 2022 which indicates statistics during the pandemic COVID-19 shows that 7 out of the top 10 causes of death in Malaysia in 2021 are NCD cases. COVID-19 is the leading cause of death at a rate of 19.8 percent. However, cumulative

cardiovascular diseases (CVD) which are ischemic heart disease, cerebrovascular disease, and hypertensive disease account for more than 20%. Diabetes mellitus, one of the risk factors for cardiovascular disease, is the top six leading causes of death in Malaysia (DOSM,2022).

2.2   Type 2 Diabetes Mellitus (T2DM)

2.2.1   Burden of Type 2 Diabetes Mellitus (T2DM)

Type 2 Diabetes Mellitus (T2DM), a significant health concern, has reached alarming levels. The epidemiological data reveals worrisome patterns that indicate a bleak future for T2DM. Globally, diabetes caused the death of 6.7 million individuals in 2021 and affected 537 million adults aged 20 to 79 years old. By 2030, this number is expected to reach 643 million, and 783 million by 2045. In 2019, around 3.9 million Malaysians, equivalent to one in every five individuals, suffer from diabetes. Additionally, the actual impact of T2DM is likely underestimated, as 232 million people, or one in every three diabetics, remain undiagnosed (NIH, 2019b). Globally, diabetes primarily affects adults aged 40 to 59 years old. It is estimated that around 240 million individuals across the globe are living with undiagnosed diabetes. This suggests that almost 50% of all adults who have diabetes are not aware of their condition. Around 90% of cases of diabetes that have not been diagnosed are found in low to middle income countries (NIH, 2019a; Dianna J Magliano (Co-chair), 2021).

Diabetes is placing an escalating financial burden on healthcare systems worldwide. The allocation of resources is primarily focused on the management of complications associated with diabetes, which frequently stem from suboptimal glycaemic control and inadequate management of concomitant cardiovascular risk

factors. When considering global healthcare expenditures associated with diabetes, which encompass country-specific expenses for 193 countries, it was estimated that at least USD 376 billion were utilized in 2010. In addition, it is anticipated that by 2030, this amount will rise to USD 490 billion. Diabetes accounts for 12% of global healthcare expenses, amounting to USD 1330 per person in 2010. Expenditure patterns vary based on geographic region, age group, gender, and income level of each country. In Malaysia, the government dedicated over 16% of the nation's healthcare budget (equivalent to approximately 2.4 billion Malaysian Ringgits) to address diabetes in 2010 (Zhang *et al.*, 2010).

2.2.2 Risk factors of T2DM

The aetiology of T2DM is multifactorial, with genetic predisposition being a significant contributing factor. However, modifiable lifestyle factors such as poor dietary habits and sedentary lifestyle are strong environmental triggers for the development of T2DM. Epidemiological research has demonstrated that a significant proportion of T2DM can be prevented by targeting modifiable risk factors such as obesity, sedentary lifestyle, and unhealthy dietary habits. However, non-modifiable risk factors such as ethnicity and family history/genetic predisposition, which have a significant genetic basis, remain influential in the development of T2DM. (Zheng *et al.*, 2018; Ojo, 2019).

2.2.3 Complications of T2DM

T2DM typically speeds up both macro- and microvascular changes, leading to long-term complications like retinopathy, neuropathy, and nephropathy. These

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complications can either be present at the time of diabetes diagnosis or develop later during the course of the disease. Research indicates that there is a delay of four to seven years between the onset of T2DM and its diagnosis. The asymptomatic stage during this delay can significantly increase morbidity by 77% (Zheng *et al.*, 2018; Babaniamansour *et al.*, 2020). Detecting diabetes at the earliest possible stage is crucial to prevent or delay complications, reduce premature mortality, and enhance quality of life. It is concerning that patients diagnosed with diabetes at a later stage, as opposed to an earlier stage, are more likely to require healthcare services due to a higher risk of diabetes-related complications. This places an additional burden on already strained healthcare systems. Insufficient access to healthcare and limitations in existing health systems often contribute to low rates of clinical diabetes diagnosis (Luna and Luyckx, 2020; Dianna J Magliano (Co-chair), 2021; Fronteira *et al.*, 2021).

2.2.4 Diagnostic test in T2DM

Different tests are available as diagnostic test for diabetes, such as fasting plasma glucose (FPG), oral glucose tolerance (OGT), or HbA1c levels. FPG is a basic blood test that measures blood glucose levels after fasting for a minimum of 8 hours. During the OGTT, the patient consumes 75 g of glucose after fasting, and they should rest and only drink plain water during the test. Diabetes is diagnosed if the 2-hour plasma glucose level is $\geq$ 11.1 mmol/L. A 2-hour plasma glucose level between 7.8-11.0 mmol/L indicates impaired glucose tolerance (IGT) or prediabetes. While the OGTT was previously considered the standard for diagnosing type 2 diabetes (T2DM), it is now recognized as being poorly reproducible and time-consuming. The American Diabetes Association (ADA) now considers HbA1c with a cut-off of $\geq$6.5% as a valid

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alternative for diagnosing diabetes compared to FPG (Sherwani *et al.*, 2016; MOH, 2020a).

There is a significant association between HbA1c levels and FPG. HbA1c testing is the preferred method for diagnosing diabetes. However, in situations where HbA1c testing is not feasible, such as during pregnancy or due to unavailable assays or circumstances limiting interpretation, FPG, 2-hour post-glucose load plasma glucose, and oral glucose tolerance tests may be used as alternative diagnostic methods. An international expert committee has recommended the use of HbA1c concentration for diagnosing diabetes due to improved test standardisation and recent data indicating its association with retinopathy. This perspective has been adopted by several countries, such as the United States, Japan, and the United Kingdom. The WHO suggests that HbA1c can serve as a diabetes diagnostic test given that there are stringent quality assurance tests, standardised assays based on international reference values, and no hindrances to precise measurement. The HbA1c test is relatively straightforward to conduct and understand since it doesn't require the patient to fast or be restricted by the time of day (Sherwani *et al.*, 2016). The key benefit of HbA1c is that it is unaffected by fluctuating blood sugar levels during illness and after meals. But there are a few things to keep into consideration. When the erythrocyte lifespan is significantly shortened in clinical conditions (such as renal anaemia with erythropoietin use, chronic and hemolytic anaemia, acute blood loss, and recent transfusion), the results will show a falsely low HbA1c level. Dialysis, chronic malaria, and liver disease might also result in a falsely low HbA1c. Iron deficiency anaemia may induce a falsely elevated HbA1c due to anticipated altered glycation rates (Weykamp, 2013; MOH, 2020a).

2.2.5   Monitoring of glycemic control in T2DM

HbA1c serves as a reliable indicator for long-term blood sugar levels and is closely linked to the likelihood of enduring diabetic complications. As a result, it is the favored method for monitoring and controlling diabetes over an extended period. By analyzing HbA1c in blood samples, one can gain insight into an individual's average blood glucose levels spanning approximately 2-3 months, aligning with the typical lifespan of red blood cells. Presently, the HbA1c test is widely recommended as a diagnostic and monitoring standard for T2DM (Weykamp, 2013; Sherwani *et al.*, 2016). Tight glycemic control is recommended for patients with T2DM, with a target HbA1C level of 7%. However, a more stringent glycemic control with a target HbA1C level of 6.5% is preferred for younger patients who are newly diagnosed and do not have comorbidities. HbA1c levels vary among diabetes patients based on their medical history and use of medication, including tablets and short- or long-term insulin. Maintaining glycemic control, optimising treatment, and ensuring patient adherence are consistently identified as the primary challenges in managing T2DM worldwide (Hammad *et al.*, 2019; Syed Soffian *et al.*, 2019). The 2010 study found that a 1% decrease in HbA1c levels could result in a 7% reduction in mortality rates and a 12-43% decrease in microvascular and macrovascular complications. Numerous studies have demonstrated a connection between glycemic control and various factors, including gender, duration of diabetes mellitus, body mass index, fasting plasma glucose, and lipid profile (Babaniamansour *et al.*, 2020). In Malaysia, it is recommended for diabetes patients with stable blood glucose levels to undergo HbA1c testing twice a year. The HbA1c level acts as a measure to evaluate the quality of care provided to diabetic patients in MOH health clinics. The Quality Assurance (QA)

indicator in Malaysia assesses the percentage of T2DM patients with HbA1c levels at or below 6.5%, with a target of 30%. Regular blood glucose testing is crucial, especially for individuals using insulin therapy, as it assists in determining the appropriate insulin dosage prior to each meal. By utilizing HbA1c readings, individuals with diabetes can estimate their average glucose level and correlate it with daily glucose monitoring (MOH, 2020a).

2.3   T2DM and CVD risk

Individuals diagnosed with diabetes are at a substantially elevated risk, approximately two to three times greater, of developing cardiovascular disease and mortality in comparison to those who do not have diabetes. In addition, it has been observed that the existence of T2DM has a detrimental impact on life expectancy, and resulting in a reduction of approximately 10 to 14 years. Cardiovascular disease is a broad term that encompasses several medical conditions, including coronary heart disease (CHD), cerebrovascular accident (CVA), peripheral artery disease (PAD), and asymptomatic individuals with "Silent" myocardial ischemia (MI) who are identified through non-invasive testing and imaging techniques that detect significant atheromatous plaques in any vascular tree (NIH, 2019a; Stoian, 2021). Several risk factors associated with cardiovascular disease are non-modifiable, such as age progression, gender, premature cardiovascular disease in the family history, and ethnicity. On the other hand, cardiovascular disease's modifiable risk factors encompass dietary habits and patterns, tobacco use, sedentary lifestyle, excessive weight or obesity, hypertension, dyslipidemia and pre-diabetes/diabetes (MOH, 2017; MOH, 2020a). The NHMS 2019 reported that there has been a rising trend in the

prevalence of cardiovascular (CV) risk factors, including hypertension, hypercholesterolemia, diabetes, overweight/obesity, and smoking. NDR 2020 revealed that a significant majority of T2DM patients also have concurrent cardiovascular (CV) risk factors which hypertension and dyslipidemia which were observed in 80.4% and 75.7% of patients, respectively.

The stratification of cardiovascular risk into three groups, namely moderate, high, and very high, has been established by the European Society of Cardiology. The moderate classification pertains to individuals who are young and have been diagnosed with diabetes for a brief period, and do not exhibit any risk factors. The high-risk category comprises individuals who have been diagnosed with diabetes for more than ten years, do not display signs of target organ damage, and possess at least one additional risk factor. Patients falling into the very high-risk category are those with a history of cardiovascular disease (CVD) and target organ injury. According to the American Association of Clinical Endocrinologists (AACE), diabetes alone presents a substantial risk (MOH, 2017; MOH, 2020a; Lee *et al.*, 2021; Stoian, 2021). Lee et al. (2021) reported that individuals with diabetes have a significantly increased risk of developing various conditions compared to those without diabetes. These include a 160% higher risk of coronary artery disease (CAD), 127% higher risk of ischemic heart disease, 56% higher risk of stroke, 2-4 times higher risk of cardiovascular disease (CVD), and 5 times higher risk of heart failure (HF). Additional factors such as smoking, physical inactivity, and alcohol consumption can contribute significantly, up to 70%, to the development of other cardiovascular risk factors like abdominal obesity, hypertension, diabetes, and hypercholesterolemia. These factors account for over 95% of acute coronary events. According to the National FINRISK studies conducted between 1972 and 2012, which involved 34,525 participants aged 30-59 years, both

men and women, a significant reduction in cardiovascular morbidity and death rates can be achieved by reducing cardiovascular risk variables. The studies showed that such reduction can result in approximately 69% decrease in men and 66% decrease in women (Jousilahti *et al.*, 2016; MOH, 2017).

During the diagnosis of prediabetes and T2DM, it is recommended to evaluate the cardiovascular risk profiles and continue assessing them at each subsequent clinical visit. Individuals classified as being in the high-risk category should receive timely treatment for their T2DM and other cardiovascular risk factors. Additionally, they should undergo more frequent monitoring to ensure effective management (Syed Soffian *et al.*, 2019). Maintaining glycemic control, optimising treatment, and ensuring patient adherence are consistently identified as the primary challenges in the global management of T2DM. Based on local data, it has been observed that a significant proportion (52.6%) of patients with Type 2 Diabetes Mellitus have received suboptimal management. This has led to inadequate glycemic control and an elevated risk of complications related to diabetes and cardiovascular disease. Type 2 Diabetes Mellitus (T2DM) is typically managed through lifestyle modifications and medications. In recent times, bariatric surgery has also emerged as a potential treatment option (Syed Soffian *et al.*, 2019; MOH, 2020a).

2.4   The Enhanced Primary Health Care

Non-communicable diseases (NCDs) are expected to remain the primary focus of healthcare services delivery across all tiers of care. The healthcare system in Malaysia is under greater strain to deliver top-notch care to patients who are dealing with NCDs and the related complications. Most people with NCDs typically receive medical care

from primary healthcare professionals as first line. The primary healthcare clinics encounter challenges in providing care for NCDs primarily due to the absence of consistent and coordinated care, inadequate organizational management of healthcare providers, extended waiting periods, limited operating hours, insufficient screening and counseling efforts, insufficient awareness regarding the significance of screening services and preventive care, and suboptimal prescription practices for treating T2DM and hypertension. These observations emphasize the significance of addressing the gaps in care within the healthcare system to effectively prevent and manage NCDs (Ministry of Health Malaysia and Harvard University TH Chan School of Public Health, 2016). Because of that, effective management of chronic diseases necessitates a collaborative approach that involves the active engagement of all relevant stakeholders, including patients, clinical healthcare practitioners, and public health policymakers for better health outcomes (Wong *et al.*, 2020).

In light of these findings, the Malaysian government has implemented measures to reinforce its commitment and realign health initiatives towards prioritizing the prevention and management of non-communicable diseases. Strategies aimed at enhancing preventive care for reducing NCDs have been specifically tailored to primary healthcare, which serves as the initial point of interaction between patients, their families, and the healthcare system. Primary healthcare plays a crucial role in providing comprehensive, coordinated, and continuous care to the entire population. To further enhance the management of NCDs within the Malaysian health system, a comprehensive care model, known as the Enhanced Primary Health Care (EnPHC) program, has been developed. This model supplements existing healthcare services by integrating public health, primary healthcare, and social support into a network that is interconnected with appropriate secondary and tertiary hospital services (Sivasampu

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et al., 2020; Wong *et al.*, 2020); Perialathan *et al.* (2021). Few initiatives were introduced based on EnPHC 3 pillars (Abdullah *et al.*, 2020; Sivasampu *et al.*, 2020; Wong *et al.*, 2020; Perialathan *et al.*, 2021):

(a)   Pillar 1: Community empowerment and health awareness

All citizen within the clinic operational area must be enrolled. A population database was established aiming for risk profiling and early intervention measures to high-risk individuals based on their respective risk levels. In the district level, the role of the community health coordinator (CHC) was established. CHC primary function is to serve as a proactive intermediary between clinics and the community. The NCD unit of the district health office is under the supervision of CHC, who holds the position of medical officer (MO). The CHC will collaborate with non-governmental organizations, KOSPEN, local organizations, and mobile health teams from clinics to facilitate health promotion and prevention, health screening, and outreach activities for enrolment and defaulter management.

(a)   Pillar 2: Person-centered care bundle

EnPHC prioritizes person-centered care as a means to encourage active, population-level initiatives for health and wellness. Healthcare professionals collaborate with patients to develop individualized care plans that are tailored to their specific needs, preferences, and health objectives. The care plans may comprise recommendations for nutrition, workout routines, medication schedules, and guidelines for self-assessment. The Integrated Specialized Services (ISS) program was implemented to provide a range of allied health services, including

occupational therapy, physiotherapy, pharmacy, NCD education, social work, dietetics, and nutrition, to patients as needed. The inter-referral mechanism was restructured via the Integrated Service System (ISS) to enhance coordination and communication between the facility and allied health services. The initiative would enable the Medical Officer to make referrals to these services and allocate more time toward the management of patients with moderate or poorly controlled conditions. The Cardiovascular Care Bundle Medication Therapy Adherence Clinic (CCBMTAC) will be implemented by pharmacists with the aim of evaluating patient adherence, performing medication assessments, encouraging adherence, and preventing medication-related complications.

(b)   Pillar 3: Integrated care network

Improved referral systems between primary healthcare centres and hospitals are necessary to ensure the seamless provision of healthcare services across various healthcare facilities and communities. Liaison officers were designated in both clinics and hospitals to oversee the coordination of patient referrals, management of referral appointment dates, and facilitation of two-way feedback between the facilities. EnPHC has developed a referral register as a monitoring mechanism for minimizing the potential risks associated with referral defaulters. EnPHC has the potential to establish a robust referral network and engage in collaborative efforts with various specialists such as endocrinologists, nutritionists, and diabetes educators to offer comprehensive treatment to individuals with diabetes. Through this, the management plan is coordinated throughout different healthcare organizations and patients have access to particular expertise when they need it.

2.5   T2DM management during pandemic COVID-19

2.5.1   Healthcare system challenges

Diabetic patients have been significantly affected by the COVID-19 pandemic, which has had repercussions on their health status as well as the healthcare system's capacity to respond efficiently. Diabetes can result in various complications if not appropriately managed. The pandemic has placed additional strain on healthcare facilities and exacerbated the challenges faced by people with diabetes, thereby increase the risk of immediate diabetic complications. (Ojo *et al.*, 2022).

2.5.2   Increased prevalence of acute diabetic complications

The surge of COVID-19 cases with a significant increase in inpatient and intensive care unit during early days of the COVID-19 pandemic has put immense pressure on healthcare systems globally, necessitating the reallocation of resources and personnel to manage the pandemic. This diversion might affect routine diabetes care and management. Patients with diabetes have faced difficulties maintaining their regular diabetes management because of restricted access to healthcare facilities, cancellation of routine or appointments, elective clinic services and reduced availability of diabetes-related supplies and medications (Al-Tawfiq *et al.*, 2020). Based on the 2020 WHO Pulse survey, it was found that 77% of countries encountered disruptions to health services to varying degrees. The services most commonly affected by these disruptions included routine immunization, diagnosis and treatment of noncommunicable diseases (NCDs), family planning and contraception, mental health disorder treatment, antenatal care, and cancer diagnosis and treatment (Al-Tawfiq *et*

al., 2020; Mobula *et al.*, 2020; Moynihan *et al.*, 2021; Tannus *et al.*, 2022). As a result, there was a decrease in in-person care, screening procedures, and delays in both diagnosis and treatment (Kapur and Hod, 2020; Palmer *et al.*, 2020).

2.6   Changes in glycemic control and cardiovascular risk during the pandemic COVID-19

People with chronic illnesses like diabetes may experience more severe effects from infections, particularly respiratory infections like COVID-19 due to their weakened immune systems. The persistent low-grade inflammation situation in DM patients offered a favorable setting for further inflammatory cytokine elevations in COVID-19 (Hu et al., 2021; Dadras et al., 2022, Rahimi et al., 2020; Harbuwono et al., 2022). Studies have demonstrated that among COVID-19 patients, diabetes is linked to an increased risk of hospitalization, admission to an intensive care unit, and mortality (IDF, 2021; Ghosh et al., 2021). Some diabetics have poor glycemic control as a result of the stress brought on by the pandemic, changes to daily routines, and restricted access to healthcare facilities. Acute consequences like diabetic ketoacidosis (DKA) or hyperglycemic hyperosmolar state (HHS) may become more likely as a result. (Kapur and Hod, 2020; Palmer *et al.*, 2020).

The fundamental basis for managing T2DM is centered on advocating for a lifestyle that encompasses a nutritious diet, consistent physical exercise, quit smoking, and maintain healthy body weight. Medication can help those with uncontrolled blood glucose levels despite lifestyle modification. Patient education is crucial to encourage self-care and empowerment (MOH, 2020a; Tannus *et al.*, 2022). Patients with diabetes face significant challenges in managing blood glucose and other metabolic parameters.

These challenges can be further complicated by changes in lifestyle and daily routines, including unhealthy dietary habits, excessive consumption of sugary foods and snacks, decreased physical activity, emotional stress, strained social relations, and altered work activities during periods of home confinement. (Ghosh *et al.*, 2020; Ruiz-Roso *et al.*, 2020a). However, patients who demonstrate improved adherence to dietary recommendations, make better food choices, prioritize sufficient nighttime sleep, and allocate more time for indoor exercise are more likely to achieve improved glycemic control (Dissanayake *et al.*, 2022).

The COVID-19 pandemic has a variety of effects on glycemic control. The variability of the findings depends on lifestyle changes during the pandemic and healthcare access. Few studies show that there are deteriorations in glycemic control among T2DM post-lockdown (Farhane *et al.*, 2021; Tewari *et al.*, 2021). But some studies reported that there are no significant changes in HbA1c among T2DM post-lockdown (Sankar *et al.*, 2020; Elmehraoui *et al.*, 2022) or no improvement in HbA1c level among T2DM post-lockdown (Dissanayake *et al.*, 2022). A sedentary lifestyle and a diet high in calories can lead to weight gain, which can negatively impact insulin sensitivity and glycemic control. There is a significant increase in body weight and BMI among T2DM post-lockdown but no significant changes in lipid profile among T2DM post-lockdown (Farhane *et al.*, 2021). MCO affects not only financially but psychologically. Quarantine and social distancing can have a psychological impact such as fear, boredom, anxiety, agitation, helplessness, mood instability, and insomnia (Palmer *et al.*, 2020; Farhane *et al.*, 2021; Bucciarelli *et al.*, 2022).

2.7 Factors influence glycemic control in T2DM

Glycemic control status is one of the key indicators of T2DM management, according to the American Diabetic Association (ADA), which demands collaboration between patients, their families, and the medical team. Glycaemic control may be impacted by a wide range of variables, including age, self-efficacy, education level, smoking status, types of medication, dietary consumption, physical activity, duration of diabetes mellitus, presence of comorbidities, and self-efficacy. Finding and addressing issues that contribute to insufficient diabetes control can help avert complications (Ahmad *et al.*, 2014; Kassahun *et al.*, 2016; Fiseha *et al.*, 2018; Hammad *et al.*, 2019; Babaniamansour *et al.*, 2020; Liu *et al.*, 2020; Martinez *et al.*, 2021).

2.7.1 Age

While the prevalence of known diabetes tends to increase with age, it is noteworthy that younger individuals exhibit poorer glycemic control. The odds ratios (OR) for age groups of 20-49 years and 50-59 years were 2.02 (95% CI, 1.52-2.70) and 1.33 (1.02-1.72), respectively, in comparison to those aged 60-69 years. According to the NHMS 2019 data, the reported prevalence of diabetes among individuals aged 35-39 years was 4.5% (95% CI: 3.04, 6.71), and it peaked at 34.3% (95% CI: 28.59, 40.50) among those aged 65-69 years (NIH, 2019a). The age discrepancy may be partially explained by a number of things. It is hypothesised that younger patients may be too preoccupied with their jobs to adhere to a healthy lifestyle and treatment. They might not see the importance of keeping their blood sugar controlled since diabetic problems, which take