PREHYPERTENSION AND ITS ASSOCIATED FACTORS AMONG TYPE II DIABETES MELLITUS PATIENTS IN KELANTAN

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by

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LIST OF SYMBOLS

*	Asterisk
<	Less than
>	More than
≤	Less than or equal to
≥	Greater than or equal to
=	Equal to
%	Percentage
Zα	Z-score associated with the level of significance
Δ	Precision of estimation
P	Proportion
α	Alpha (significance level)
B	Beta regression coefficient
m	Ratio of independent variable
n	Sample size
p	*p*-value

LIST OF ABBREVIATIONS

aOR	Adjusted odds ratio
ACCORD	Action to Control Cardiovascular Risk in Type II Diabetes trial
ARIC	Atherosclerosis Risk in Community
BMI	Body mass index
CI	Confidence interval
CPG	Clinical Practice Guideline
CVD	Cardiovascular disease
DASH	Dietary Approach to Stop Hypertension
DM	Diabetes Mellitus
DOSM	Department of Statistics Malaysia
DBP	Diastolic blood pressure
HbA1c	Glycated haemoglobin
HR	Hazard ratio
HDL-C	High-density lipoprotein cholesterol
IHME	Institute For Health Metrics and Evaluation
INVEST	International Verapamil Trandolapril Study
JEPeM USM	Jawatankuasa Etika Penyelidikan Manusia Universiti Sains Malaysia
JNC 7	7th Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
KOSPEN	*Komuniti Sihat, Perkasa Negara* program
LDL-C	Low-density lipoprotein cholesterol
LR	Likelihood Ratio
MOH	Ministry of Health
NCD	Non-communicable diseases
NDR	National Diabetes Registry
NHMS	National Health and Morbidity Survey
NMRR	National Malaysia Research Registry
MLR	Multiple Logistic Regression
ONTARGET	Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial
OR	Odds ratio

PEN	Package of Essential Noncommunicable Disease Interventions for Primary Health Care
PLOS	Public Library of Science
PROGRESS	Perindopril Progression Against Recurrent Stroke trial
RAAS	Renin-angiotensin-aldosterone system
RCT	Randomized controlled trial
ROC	Receiver Operating Characteristic
SBP	Systolic blood pressure
SD	Standard deviation
SGLT 2	sodium-glucose cotransporter 2
SNS	Sympathetic nervous system
IBM SPSS	International Business Machines Corporation Statistical Package for Social Sciences
T2DM	Type II Diabetes Mellitus
TC	Total cholesterol
TG	Triglyceride
TyG	Triglyceride glucose index
TyG-BMI	Triglyceride glucose-BMI index
WC	Waist circumference
WHO	World Health Organization

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PRAHIPERTENSI DAN FAKTOR-FAKTOR BERKAITAN DALAM KALANGAN PESAKIT KENCING MANIS JENIS DUA DI KELANTAN

ABSTRAK

Latar Belakang: Prahipertensi ialah keadaan di mana bacaan tekanan darah sistolik antara 120 sehingga 139 mmHg dan/atau tekanan darah diastolik antara 80 sehingga 89 mmHg. Pesakit kencing manis jenis dua (T2DM) yang mengalami prahipertensi menghadapi risiko morbiditi dan mortaliti kardiovaskular yang lebih tinggi berbanding pesakit T2DM yang normotensif. Walau bagaimanapun, ramai pesakit T2DM masih tidak menyedari status prahipertensi mereka dan peningkatan risiko penyakit kardiovaskular akibat prahipertensi.

Objektif: Kajian ini bertujuan untuk menentukan pembahagian prahipertensi dan faktor-faktor berkaitan dalam kalangan pesakit T2DM di Kelantan bagi tahun 2022.

Metodologi: Kajian keratan rentas ini dijalankan dari bulan Disember 2023 hingga Jun 2024 menggunakan data sekunder daripada set data audit klinikal *National Diabetes Registry* (NDR) Kelantan bagi tahun 2022. Data pesakit T2DM yang berusia lebih daripada 18 tahun dan dinyatakan tidak menghidapi hypertensi daripada daftar tersebut dikumpulkan menggunakan proforma dan dianalisa menggunakan perisian IBM SPSS versi 28.

Keputusan: Terdapat 8657 set data audit klinikal pesakit T2DM dalam NDR Kelantan bagi tahun 2022, yang mana 825 set data pesakit memenuhi kriteria kajian dan dimasukkan dalam kajian. Analisis deskriptif dan regresi logistik berbilang telah dijalankan. Terdapat 606 (73.5%) pesakit T2DM yang prahipertensi dengan usia purata (SD) 55.8 (11.30) tahun, majoriti adalah pesakit perempuan seramai 402 pesakit (66.3%) dan berbangsa Melayu seramai 585 pesakit (96.5%). Hanya 41 (6.8%) pesakit

adalah perokok manakala 330 (54.5%) pesakit menghidapi dislipidemia. Majoriti pesakit adalah berlebihan berat badan [254 pesakit (41.9%)] dan obes [215 pesakit (35.5%)] dengan 370 (61.1%) pesakit mempunyai lilitan pinggang yang abnormal. Purata (SD) tahap HbA1c adalah 8.31% (2.21) manakala 87 (14.4%) pesakit mengalami mikroalbuminuria. Faktor-faktor berkaitan yang signifikan dengan prahipertensi dalam kajian ini ialah umur (aOR 1.02; 95% CI: 1.003, 1.03; p = 0.012), jantina (aOR 1.54; 95% CI: 1.10, 2.15; p = 0.013) dan merokok (aOR 2.19; 95% CI: 1.02, 4.73; p = 0.045).

Kesimpulan: Prahipertensi dalam kalangan pesakit T2DM di Kelantan pada tahun 2022 adalah tinggi. Selain faktor yang tidak boleh diubah seperti umur dan jantina, merokok didapati mempunyai hubungan yang signifikan dengan prahipertensi dalam kalangan pesakit T2DM justeru menekankan kepentingan promosi berhenti merokok untuk pesakit T2DM bagi mengelakkan terjadinya prahipertensi.

KATA KUNCI:

prahipertensi, kencing manis, faktor risiko, hypertensi

PREHYPERTENSION AND ITS ASSOCIATED FACTORS AMONG TYPE II DIABETES MELLITUS PATIENTS IN KELANTAN

ABSTRACT

Background: Prehypertension is defined by systolic blood pressure ranging from 120 to139 mmHg and/or diastolic blood pressure of 80 to 89 mmHg. Type II Diabetes Mellitus (T2DM) patients with prehypertension face higher risks of cardiovascular morbidity and mortality compared to normotensive T2DM patients. However, many T2DM patients remains unaware of their prehypertensive status and the associated increased CVD risks.

Objective: This study aims to determine the proportion of prehypertension and its associated factors among Type II Diabetes Mellitus patients in Kelantan for year 2022.

Methodology: This cross-sectional study was conducted from December 2023 to June 2024 using secondary data from Kelantan National Diabetes Registry (NDR) clinical audit datasets for the year 2022. Data of T2DM patients who were more than 18 years old and documented not hypertensive in the registry was collected using a proforma and analysed using IBM SPSS version 28 software.

Results: There were 8657 T2DM patients clinical audit datasets in Kelantan NDR for the year 2022, of which, 825 patient datasets fulfilled the study criteria and were included in the study. Descriptive and multiple logistic regression analysis were performed. The proportion of prehypertensive T2DM patients was 73.5% (606 patients) with a mean (SD) age of 55.8 (11.30) years old, majority being the female patients at 402 patients (66.3%) and of Malay ethnicity at 585 (96.5%) patients. Only 41 (6.8%) patients were smoker while 330 (54.5%) patients had dyslipidaemia. Majority of patients were overweight [254 (41.9%) patients] and obese [215 (35.5%)

patients] with 370 (61.1%) patients having abnormal waist circumference. The mean (SD) of HbA1c level was 8.31% (2.21) while 87 (14.4%) patients experienced microalbuminuria. Significant association with prehypertension was found for age (aOR 1.02; 95% CI: 1.003, 1.03; $p = 0.012$), sex (aOR 1.54; 95% CI: 1.10, 2.15; $p = 0.013$) and smoking (aOR 2.19; 95% CI: 1.02, 4.73; $p = 0.045$)

Conclusion: There was a high proportion of prehypertension among T2DM patients in Kelantan in the year 2022. Besides non-modifiable factors age and sex, smoking was significantly associated with prehypertension among T2DM patients thus highlighting the importance of smoking cessation promotion for T2DM patients to prevent the development of prehypertension.

KEYWORDS:

prehypertension, diabetes mellitus, risk factors, hypertension

CHAPTER 1

INTRODUCTION

1.1 Diabetes and prehypertension

The World Health Organization (WHO) had reported that the prevalence of diabetes has risen multiple folds from 108 million to 422 million from 1980 till 2014 (WHO, 2023b). Diabetes is one of the four non-communicable diseases contributing to the equivalent of 70% of annual global deaths (WHO, 2023a). It rarely exists as a single disease in a patient; its most common comorbidity being hypertension. The unfortunate presence of both hypertension and diabetes in an individual increases their risk of cardiovascular morbidity and mortality (Khangura *et al.*, 2018). Chen *et al.* (2011) in his retrospective cohort study of four-year duration among 1145 Framingham study participants recorded 72% increase in the risk of all-cause mortality and 57% increase in the risk of any cardiovascular disease (CVD) event for diabetic patients who were also diagnosed with hypertension.

In Malaysia, the key findings of the latest National Health Morbidity Survey (NHMS) 2024 reported that the prevalence of Type II Diabetes Mellitus (T2DM) is at 15.6% while the prevalence of hypertension is 29.2% for the general population in the year 2023 (NIH, 2024). However, when focusing among T2DM patients specifically, National Diabetes Registry (NDR) Report 2020 revealed that hypertension prevalence was reported at a whopping 80.0% (MOH, 2021). This is highly concerning considering the increased risk of cardiovascular diseases mentioned earlier.

Recognizing these increased risks and complications of the presence of both T2DM and hypertension in an individual, the 6th Edition of the Malaysian Clinical Practice Guidelines (CPG): Management of Type II Diabetes Mellitus has clearly defined and outlined the management of hypertension among T2DM patients (MOH,

2020). A persistent reading in systolic blood pressure (SBP) of more than 140 mmHg and diastolic blood pressure (DBP) of more than 90 mmHg is the cut-off point for both diagnosing and initiating pharmacological treatment for hypertension in a T2DM patients.

While the previous NHMS 2019 did report a 37.0% prevalence of prehypertension among general population (NIH, 2020), both the NHMS 2019 and NDR Report 2020, however, did not report on the prevalence of prehypertension among T2DM patients. Considering the alarmingly high prevalence of hypertension among T2DM patients compared to the general population as well as the considerably high prevalence of prehypertension among general population, it is entirely plausible that the prevalence of prehypertension among T2DM would also follow the same pattern.

If the importance of hypertension control in T2DM patients is indisputable, the effort to prevent it from even occurring in the first place is just as, if not more, paramount. Especially so when a cohort study from 2004 till 2015 in Korea among 115,456 middle-aged and elderly participants with prehypertension showed that diabetes mellitus was one of the best predictors for progression to hypertension with adjusted hazard ratio HR of 1.30; 95% CI: 1.24,1.36 for females and adjusted HR of 1.50; 95% CI: 1.44, 1.56 for males (Yu *et al.*, 2020).

1.2   Prehypertension

The 7th Report of Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), in the effort to increase awareness for hypertension prevention among health care providers as well as public, introduced the term prehypertension into blood pressure classification in 2003 (Chobanian *et al.*, 2003). Blood pressure range for prehypertension was defined as systolic BP of 120 to 139 mm Hg or a diastolic BP of 80 to 89 mm Hg. No pharmacological treatment was recommended for individuals within the prehypertension range. Instead, JNC 7 outlined detailed lifestyle modifications for the general population with prehypertension to prevent their subsequent progression into hypertension.

1.3   Problem Statement and Rationale of the Study

Referencing the described range of prevalence of hypertension among T2DM patients (80.0%) reported by NDR Report 2020, the 59.4% prevalence of prehypertension among T2DM patients in a population study by Zhang *et al.* (2006) as well as the prevalence of prehypertension among general population (37.0%) by NHMS 2019, T2DM population who do not have an established diagnosis of hypertension must not be nonchalant and complacent with their risk of developing prehypertension and subsequently hypertension. These T2DM patients could very well be within the prehypertension range hence unknowingly exposing them to the devastating increased risks cardiovascular morbidity and mortality mentioned above.

Acknowledging this, appropriate and tailored lifestyle modifications, and management for prehypertension among T2DM patients would be a worthwhile endeavour. While the 6th edition of the T2DM CPG is very clear in the definition and

management of hypertension among T2DM patients, for T2DM patients who do not have hypertension diagnosis, the CPG only denotes those patients to be in no need of any pharmacological treatment for their blood pressure control with no further emphasis regarding lifestyle modifications for prevention of prehypertension. While JNC 7 Report did outline the lifestyle modifications for the general population with prehypertension; for T2DM patients, however, a more tailored lifestyle modification for prehypertension prevention would be more beneficial.

Therefore, this study aims to highlight the burden of prehypertension among T2DM patients in Kelantan and determine the associated factors. By detection of the factors contributing to prehypertension in T2DM patients, this study may illustrate the burden and thus the importance of devising the appropriate, targeted, and tailored lifestyle modifications and intervention for prehypertension among T2DM patients.

1.4   Research Questions

1. What is the proportion of prehypertension among Type II Diabetes Mellitus patients in Kelantan?
2. What are the associated factors of prehypertension among Type II Diabetes Mellitus patients in Kelantan?

1.5   Research Objectives

1.5.1   General Objective

To study the proportion of prehypertension and its associated factors among Type II Diabetes Mellitus patients in Kelantan for the year 2022

1.5.2   Specific objectives

1. To describe the proportion of prehypertension among Type II Diabetes Mellitus patients in Kelantan for the year 2022

2. To determine the associated factors of prehypertension among Type II Diabetes Mellitus patients in Kelantan for the year 2022

1.6   Research Hypothesis

There is a significant association between sociodemographic and clinical factors and prehypertension among Type II Diabetes Mellitus in Kelantan.

CHAPTER 2

LITERATURE REVIEW

Search of papers and literatures pertaining to the study was conducted using online search engines that include PubMed, Science Direct, Scopus, PLOS, and Google Scholar. Various searching strategies were applied including using Boolean operators; "AND", "OR" and "NOT". The keywords used were prehypertension, diabetes mellitus, risk factors, hypertension.

2.1   Prehypertension among T2DM patients

There is a lack of study specifically on prehypertension in T2DM populations; with most studies focusing more on either prehypertension in general population or hypertension in diabetic populations. For prevalence of prehypertension in T2DM patients, one study by Zhang *et al.* (2006) reported the prevalence among diabetic patients compared to their non-diabetic counterparts. It was a population-based study involving 2629 participants in southwestern Oklahoma, central Arizona, north and south Dakota in the United States of America (USA) which recorded the prevalence of prehypertension to be higher in T2DM populations (59.4%) compared to their non-diabetic counterparts (48.2%).

Most other studies reported on prehypertension prevalence among general population, among which including the studies by Egan and Stevens-Fabry (2015) and Rahman *et al.* (2018). Egan and Stevens-Fabry (2015) reported in their systematic review a range of 22% to 38% prevalence of prehypertension for Taiwan, Japan, Korea and Germany, and a slightly higher prevalence at 52.1% in Iran. In Bangladesh, on the other hand, a comparable prevalence of prehypertension in urban and rural population of 44.5% and 41.5% respectively was demonstrated (Rahman *et al.*, 2018). From these

studies, it seems agreeable that a substantial prevalences of prehypertension among both diabetic and non-diabetic population were observed.

T2DM individuals with prehypertension were reported to have approximately a four-fold increased risk for cardiovascular events in comparison to those with normal BPs and normal glucose tolerance (Zhang *et al.*, 2006). Huang *et al.* (2020) in a more recent study using data of 26,070 participants from National Health and Nutrition Examination Surveys (NHANES) demonstrated similar increased risks in multivariable adjusted hazard ratio (HR) for cardiovascular mortality which were 1.40 (0.92, 2.14), 2.21 (1.12, 4.38) and 2.87 (1.65, 4.99) (p<0.001 for trend), for those with diabetes alone, prehypertension alone, and with both diabetes and prehypertension respectively. Furthermore, the study also reported the HRs for all-cause mortality were 1.08 (0.95, 1.23), 1.26 (0.98, 1.62) and 1.67 (1.38, 2.03) (p<0.001 for trend) respectively. These findings highlighted the highest risks were observed in the group with both diabetes and prehypertension.

2.2   Associated factors of prehypertension among diabetic patients

Many risk factors might contribute to prehypertension among T2DM patients. However, most studies on prehypertension were done among the general population, while among T2DM population, studies were more focused on hypertension. Studies focusing specifically on associated factors for prehypertension among T2DM population were notably lacking. Nonetheless, most of available studies would go on to report on multiple similar, or at least comparable, significant associated factors for prehypertension in general population and T2DM patients as well as hypertension in general population and T2DM patients.

2.2.1   Sociodemographic and lifestyle risk factors

One of the most prevailing associated factors reported is age. Ismail *et al.* (2022) found statistically significant associations with hypertension in the age group of 40-59 years old (aOR 2.82; 95% CI: 2.15, 3.69) and 60 years and above (aOR 6.92; 95% CI: 4.83, 9.92) of T2DM patients. This is also shown in a study among general population by Mahadir Naidu *et al.* (2019) where individuals with blood pressure within the prehypertensive level showed a gradual increase in their chances of having hypertension with age where higher age groups (30 – 39-year-olds, 40 – 59-year-olds, and 50 – 59-year-olds) had higher percentage of hypertension from 40% to 400% relative to those in the youngest age group (18–29-year-olds). Similarly, a study by Abougalambou and Abougalambou (2013) also indicated that hypertension was positively associated with age (p = 0.040). This is further supported by a study by Song *et al.* (2018) who found similar association between age and prehypertension status (aOR 1.01; 95% CI: 1.00,1.02).

Mahadir Naidu *et al.* (2019) and Rafan *et al.* (2018) found in their studies that male sex was significantly associated with prehypertension compared with female sex (aOR 2.74; 95% CI: 2.41, 3.12) and (aOR 4.44; 95% CI: 1.58, 12.44; p < 0.005) respectively. Being Malay (aOR 1.21; 95% CI: 1.02, 1.44) was also shown to be significantly associated with prehypertension when compared to Chinese, Indian other ethnicities (Mahadir Naidu *et al.*, 2019). In a population based study in Singapore, it was found that for all three ethnicities Chinese, Malay, and Indian; high-blood glucose level, high-HbA1c and high-BMI were all significant associated factors for prehypertension with aOR 1.42; 95% CI: 1.10, 1.83, aOR 1.53; 95% CI 1.05, 2.24, aOR 1.49; 95% CI: 1.13, 1.98 for high-glucose; aOR 3.50; 95% CI: 1.01, 12.18, aOR 3.72; 95% CI: 1.29, 10.75, aOR 2.79; 95% CI: 1.31, 5.94 for high-HbA1c; and aOR

1.86; 95% CI: 1.34, 2.56, aOR 2.96; 95% CI: 2.10, 4.18, aOR 1.68; 95% CI: 1.28, 2.20 for high-BMI, respectively for each race (Chiang *et al.*, 2013). Other than older age, male sex and Malay ethnicity, Mahadir Naidu *et al.* (2019) also found other significant associated factors of higher risk of prehypertension for those who were never married, lived rurally, from lower socio-economic status, diabetes, hypercholesterolaemia and excessive body weight.

Next, family history of hypertension could also be a significant factor for prehypertensive as evidenced by adjusted hazard ratio (HR) of 1.44; 95% CI: 1.37, 1.52 in a study by Yu *et al.* (2020). Song *et al.* (2018) in their study reported family history of cardiovascular disease was also a significant associated factor for prehypertension (aOR: 1.52; 95% CI: 1.14, 2.02). The study also found smoking as a significant associated factor of prehypertension among the general population (aOR 1.67, 95% CI: 1.22, 2.29). Other significant associated factors listed in their study include general obesity (aOR 1.51, 95% CI: 1.15, 1.97).

2.2.2   Clinical risk factors

Two studies reported on high body mass index (BMI) association with prehypertension. Zhang *et al.* (2011) reported 26.7% overweight/obesity prevalence in prehypertensive population vs 15.9% non-prehypertensive population. Rahman *et al.* (2018) reported increasing prevalence of prehypertension with obesity among both Bangladeshi rural and urban populations aOR 4.6; 95% CI: 3.1, 7.0 and aOR 3.0; 95% CI: 1.5, 5.9 respectively. Abougalambou and Abougalambou (2013) also supported the significant association between BMI (p = 0.027) and hypertension status.

Chockalingam *et al.* (2005) in their studies showed a significant association between abnormal waist circumference and prehypertension with aOR 1.05; 95% CI:

1.03, 1.07. Anari *et al.* (2017) also demonstrated that central obesity was an important associated factor for hypertension in his study. Closely related, for association of dyslipidaemia with prehypertension, besides Mahadir Naidu *et al.* (2019), Ismail *et al.* (2022) also reported a significant association with aOR 1.57; 95% CI: 1.27, 1.93. Similar significant association was also observed by Zhang *et al.* (2011) in a study of prehypertension among general population.

Chiang *et al.* (2013) in a study in Singapore also revealed significant association between high-level HbA1c and hypertension. HbA1c was also reported to be positively associated with hypertension by Abougalambou and Abougalambou (2013). Finally, in a study in Tianjin, China, in the prehypertensive group, it was shown that the diabetes subgroup had a significant association with microalbuminuria, and the adjusted odd ratio of the diabetes subgroup to the normoglycaemia subgroup was aOR 2.68; 95% CI: 1.54, 4.67; *p*<0.001 (Wang *et al.*, 2018).

2.3   Conceptual framework

Factors that might contribute to higher risk of developing prehypertension among T2DM patients could be grouped into sociodemographic characteristics, lifestyle factors and clinical characteristics. However, due to limited availability of data, only the highlighted risk factors of prehypertension were studied. The outcome of this study is the prehypertension status among the T2DM patients in the 2022 Kelantan NDR.
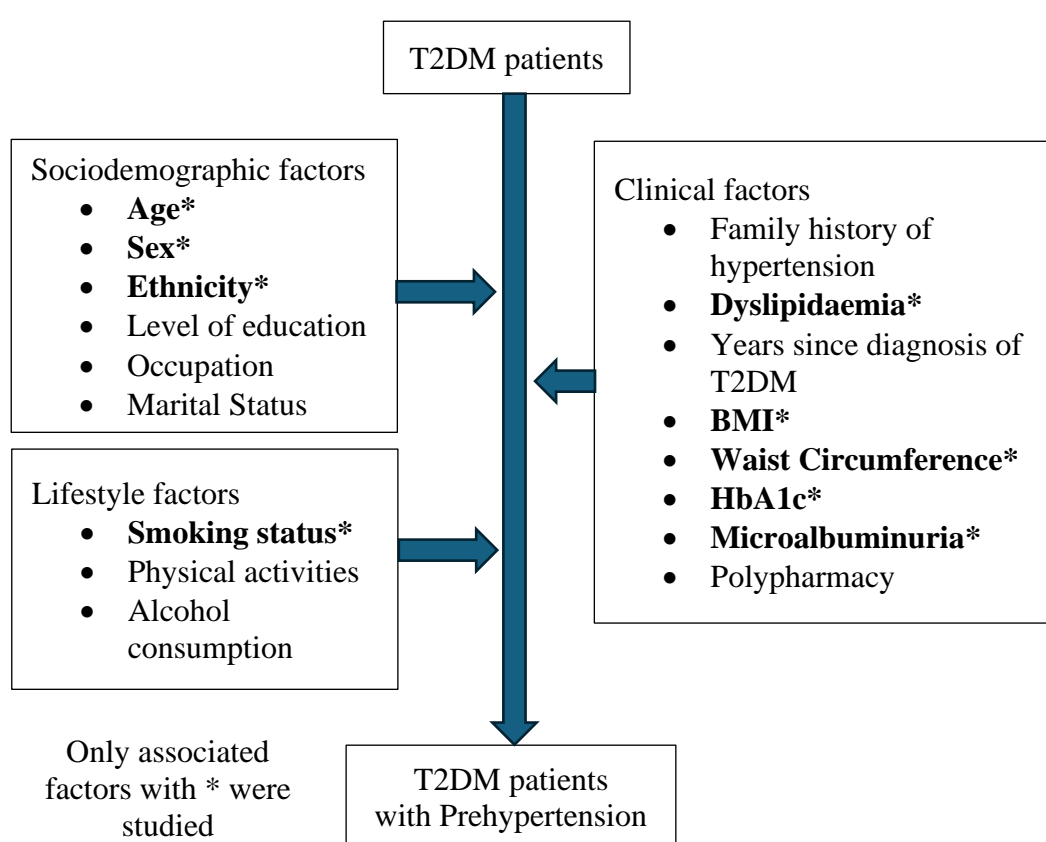
Figure 2.1 Conceptual Framework of the study

CHAPTER 3

METHODOLOGY

3.1   Study design

This study applied a cross-sectional study design using secondary data from the Kelantan National Diabetes Registry (NDR) for the year 2022.

3.2   Study duration

This study was conducted from December 2023 till June 2024.

3.3   Study location

The study was conducted at Non-Communicable Diseases (NCD) Unit, Kelantan State Health Department for data collection.

3.4   Study population

3.4.1   Reference population

The reference population for this study was T2DM patients in Kelantan.

3.4.2   Source population

The source population of this study was T2DM patients registered in Kelantan NDR 2022

3.4.3   Sampling population

The sampling population was T2DM patients registered in the Kelantan NDR 2022 who fulfilled the inclusion and exclusion criteria.

3.5   Subject criteria

3.5.1   Inclusion criteria

1. Data of all T2DM patients aged more 18 years old

2. Data noted as "no" for variable Hypertension

3.5.2   Exclusion criteria

1. Missing data for variable "Hypertension"

2. Data noted as "no" for variable Hypertension however blood pressure was reported within hypertensive range i.e., SBP equal to or greater than 140 mmHg or DBP equal to or greater than 90 mmHg

3. Missing data more than 30% of variables per person data

3.6   Sample size determination

The sample size was calculated based on the study specific objectives.

3.6.1   Sample Size Calculation for Specific Objective 1

To determine the proportion of prehypertension among T2DM patients in Kelantan for the year 2022, the single proportion formula for estimation of sample size was used,

$$n = \left(\frac{Z_\alpha}{\Delta} \right)^2 \times P(1\text{-}P)$$

Where:

Z_α = Level of confidence corresponding to critical Z value of $\alpha/2$ = 1.96

Δ = Precision of estimation = 0.05

P= Zhang *et al.,* (2006) reported the prevalence of prehypertension among T2DM patients in a cohort study was 59.4%.

The estimated sample size to determine the proportion of prehypertension among T2DM is 465 participants, including the consideration of 20% missing data.

3.6.2   Sample Size Calculation for Specific Objective 2

The estimated sample size for specific objective two was determined for several variables associated with prehypertension among T2DM patients using Power and Sample Size calculation software to compare two independent proportion where:

α = value of the standard normal distribution cutting of probability α = 0.05 (two tailed)

Power = power of study 0.80 = 80% power

m = ratio unexposed / exposed

P0 = proportion of associated factors (unexposed) of prehypertension

P1 = estimated proportion of associated factor (exposed) of prehypertension

Table 3.1 Sample size calculation for Specific Objective 2

Variables	α	Power	P0*	P1	m	n	Sample size (2n + 20% missing data)	Literature*
Male sex	0.05	0.80	0.32	0.50	1	116	279	Zhang *et al.*, 2011
Obesity (yes)	0.05	0.80	0.39	0.60	2	198	248	Ismail *et al.*, 2023
Waist circumference (abnormal)	0.05	0.80	0.23	0.50	3	124	155	Rafan *et al.*, 2018

In conclusion, based on the above calculations, the largest sample size required to answer the study objectives was from sample size for objective one (n= 465).

3.7   Sampling method

Simple random sampling method was supposed to be applied in selection of the study subjects from 8657 data from Kelantan National Diabetes Registry (NDR) 2022 based on the sample size estimation using a random function in the Microsoft Excel. However, after application of inclusion and exclusion criteria, the sample data of T2DM patients with no hypertension was considerably small, hence no sampling method was applied to ensure an adequate sample of non-hypertensive T2DM patients to accomplish specific objective two.

3.8   Research tools

3.8.1   National Diabetic Registry (NDR) from Kelantan State Health Department

National Diabetes Registry (NDR), which begins in 2009 and is then later monitored via a web-based data collection system that has been active since 2011, is a patient registry that collects socio-demographic information, clinical and outcome data of all T2DM patients managed in Ministry of Health (MOH) health clinics and selected hospitals. The NDR audit team conducts annual audit on randomly selected clinical datasets by thorough review and validation of available data thus ensuring completeness and high data quality for subsequent analysis and interpretation.

This study used the Kelantan NDR annual clinical audit datasets for the year 2022 in view of NDR data collection from the year 2019 through 2021 was impacted by the COVID-19 pandemic.

3.8.2   Checklist Proforma

A checklist proforma was designed and used to obtain the variables required for this study, which were age, sex, ethnicity, smoking status, waist circumference, body mass index (BMI), dyslipidaemia status, systolic blood pressure (SBP), diastolic blood pressure (DBP), HbA1c level, and microalbuminuria (Appendix A).

3.9   Operational definition

3.9.1   Prehypertension

This study used the definition of prehypertension by 7th Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7 Report) (Chobanian *et al.*, 2003).

- Systolic BP ranges 120 -139 mmHg and/or
- Diastolic BP ranges 80 – 89 mmHg

The blood pressure reading used in this study was the single latest blood pressure reading recorded during the previous medical examination follow-up for the patient.

3.9.2 Body mass index (BMI)

BMI categories are defined based on CPG on Management of Obesity Second Edition, 2023 (MOH, 2023b)

Table 3.2 Classification of BMI

Classification	BMI (kg/m^2)
Underweight	< 18.5
Normal Range	18.5 – 22.9
Overweight	≥23
Pre-Obese	23.0 – 27.4
Obese I	27.5 – 34.9
Obese II	35.0 – 39.9
Obese III	≥ 40.0

3.9.3 Waist Circumference

Abnormal waist circumference is defined based on CPG on Management of Obesity Second Edition, 2023 (MOH, 2023b).

1. Male: >90cm

2. Female: > 80cm

3.10 Data Collection Method

This study utilised secondary data collection from 2022 Kelantan National Diabetes Registry - Diabetes Clinical Audit with written permission from the Director of the State Health Department of Kelantan (Appendix B). Data was extracted at Non-Communicable Disease (NCD) Unit, Kelantan State Health Department using the proforma to ensure relevance and confidentiality. All cases were identified by code numbers without personal identifiers. Data was imported from Microsoft Excel and

then exported to IBM Statistical Package for Social Sciences (SPSS) version 28.0 for further statistical data analysis.

3.11   Statistical analysis

Data entry and analysis were carried out using IBM Statistical Package for Social Sciences (SPSS) version 28.0. After data was converted from Microsoft Excel datasheet into SPSS datasheet, the data was explored, checked, and cleaned. Numerical variables were checked for normality distribution of data.

3.11.1   Descriptive statistics

Socio demographic (age, sex and ethnicity) and clinical characteristics (smoking status, waist circumference, BMI, dyslipidaemia status, HbA1c level, and microalbuminuria) were tabulated for descriptive characteristics. Numerical variables were normally distributed and described in mean and standard deviation (SD) while categorical variables were presented as frequency (n) and percentage (%).

The proportion of prehypertension and normotension among non-hypertensive diabetic patients in Kelantan Diabetes Registry 2022 were depicted in a bar graph with values indicated in percentage (Figure 4.2).

3.11.2   Associated Factors of Prehypertension among T2DM patients

The statistical analysis was done using simple and multiple logistic regression. Simple logistic regression was used to select preliminary variables of associated factors of prehypertension among T2DM patients. The prehypertension status of each study participant was categorized as prehypertension or normotension based on the operational definition. The outcome was a binary variable coded as "0" for normotension and "1" for prehypertension.

The variables explored were age, sex, ethnicities, smoking status, waist circumference, BMI, dyslipidaemia status, HbA1c level, and presence of microalbuminuria. Age and HbA1c level were analysed as continuous variables whereas sex, ethnicity, smoking status, dyslipidaemia status, BMI, waist circumference and microalbuminuria were analysed as categorical variables. Sex was categorized as "male" and "female" while for smoking status, dyslipidaemia status and microalbuminuria; "yes" and "no" categories were used based on the registry data entry. Ethnicity was collapsed into three groups "Malay" and "Chinese" and "Others" as the number of study participants with ethnicities Chinese, Indian, Bumiputra Sabah, Orang Asli Peninsular, foreign nationals and others were either non-existent or too small. BMI was categorized as either "underweight", "normal", "overweight" or "obese" as per operational definition. Waist circumference was categorised as "normal" or "abnormal". From univariate analysis, variables with p-value of less than 0.25; or of any clinical importance were selected for multiple logistic regression.

Multiple logistic regression (MLR) was used to identify associated risk factors of prehypertension among T2DM patients. Preliminary main effect model was obtained after comparing model using Backward and Forward LR models. Multicollinearity was checked using correlation matrix to determine any multicollinearity between plausible variables. All plausible two-way interactions between variables were also checked. The preliminary final model was obtained.

The fitness of the model was tested using Hosmer and Lemeshow goodness of fit test. The classification table and area under receiver operating characteristics (ROC) curve were also used to determine the fitness of the model. The Hosmer and Lemeshow goodness of fit test with p-value of more than 0.05 indicates that the model is fit. Classification table with overall correctly classifies percentage of

80% and above; and area under ROC curve of 0.7 and above indicate that the model was fit.

The final model was determined by enter forced method. The adjusted odd ratio (aOR) and 95% CI were calculated and used as a measure of strength of association between the outcome variable and the risk factors. The level of significance was set at p-value of less than 0.05.

3.12   Ethical considerations

The main ethical considerations in this study were the ethical access and usage of the secondary data from Kelantan State Diabetes Registry for year 2022 and the responsibility of researchers to maintain confidentiality of the data used in the study. Written permission was obtained from Director of Kelantan's State Health Department for access and usage of the data (Appendix B). All data obtained excluded any personal identifiers to ensure confidentiality and privacy. All researchers involved had declared no conflicts of interest in relation to the study. Ethical clearance approval was obtained from Jawatankuasa Etika Penyelidikan Manusia Universiti Sains Malaysia (JEPeM), University Sains Malaysia (USM/JEPeM/KK/23110857) (Appendix C) and Medical Review and Ethical Committee from National Institute of Health, Ministry of Health Malaysia NMRR ID- 23-03358-NLF (IIR) (Appendix D).

3.13   Flow of study

      The study started with collection of data from Kelantan State National Diabetes Registry for clinical audit year 2022. Data that fulfilled the study criteria were chosen and entered to the statistical software IBM SPSS version 28 for analysis followed by thesis write-up and submission.
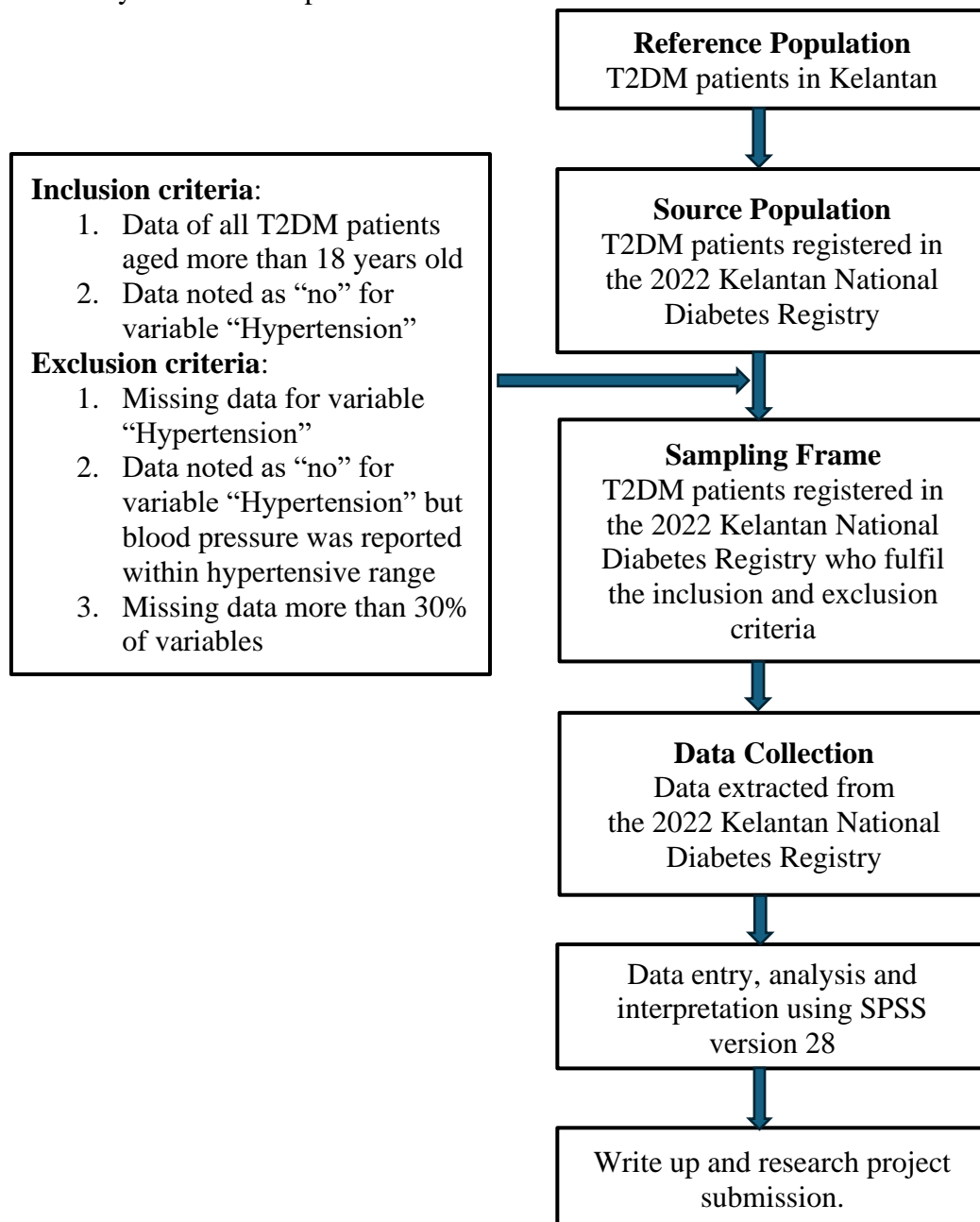

Figure 3.1 Study flowchart

CHAPTER 4

RESULT

4.1   Sociodemographic and clinical characteristics of T2DM in Kelantan National Diabetes Registry clinical audit year 2022

There were 8657 T2DM patients' datasets registered in the 2022 Kelantan National Diabetes Registry - Diabetes Clinical Audit. From these, 1685 patients (19.5%) did not have a hypertension diagnosis.

Among the 1685 patients who did not have a hypertension diagnosis during the clinical audit, 552 patients' datasets had more than 30% missing data of the variables in this study leaving only 1133 patients' datasets fulfilling the study criteria. However, 308 (27.2%) of these patients were noted to have systolic blood pressure and/or diastolic blood pressure readings within the hypertensive range of more or equal to 140mmHg for systolic blood pressure and more or equal to 90mmHg for diastolic blood pressure. These patients were categorized as hypertensive in this study and thus excluded from the study. Hence, the final number of patients in this study was 825 patients (Figure 4.1).
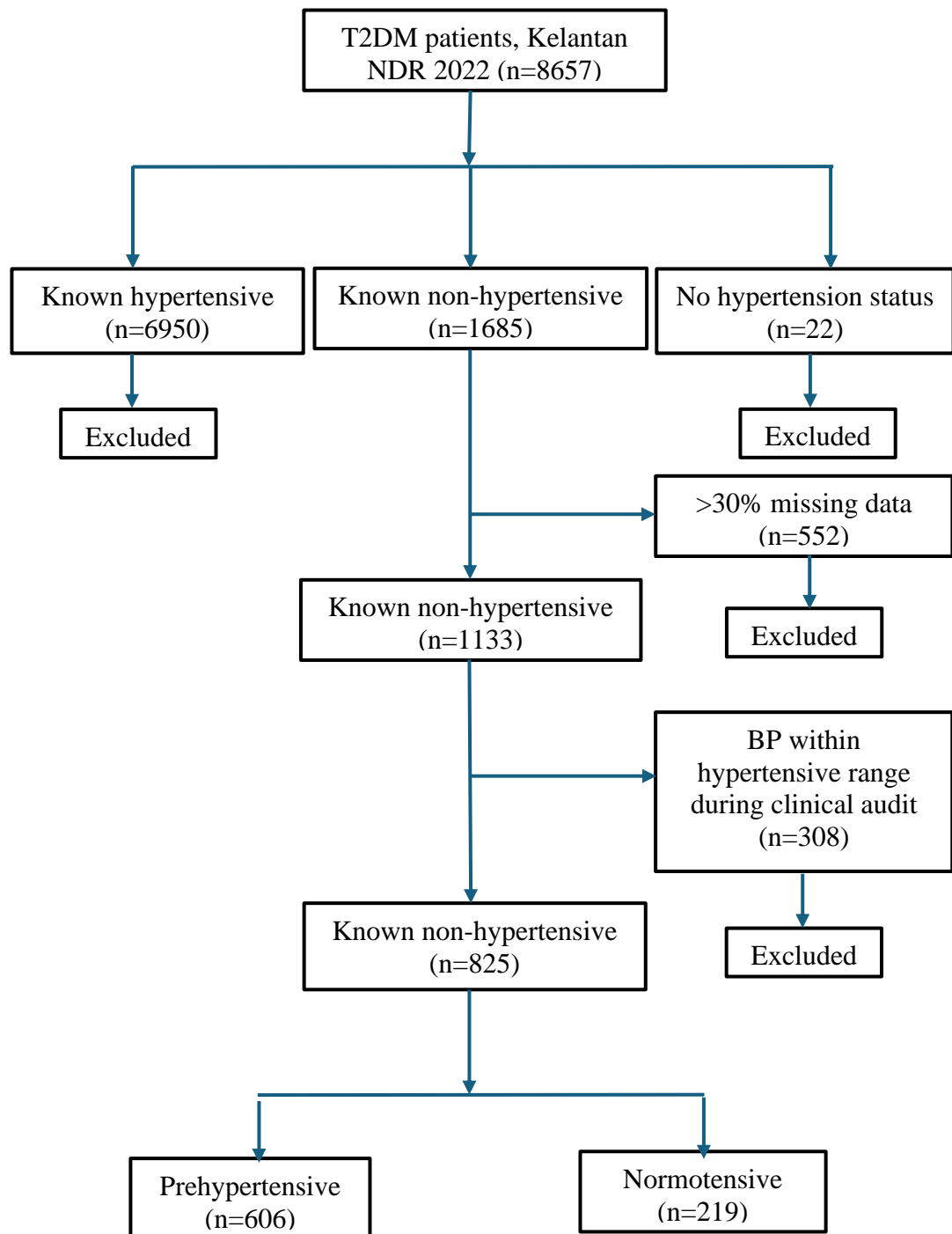
Figure 4.1 Sample size from total study participants in Kelantan NDR 2022

The age of patients ranged between 20 to 85 years old with a mean (SD) age of 55.3 (11.34) years. The study participants comprised of 533 (64.6%) female patients and 292 (25.4%) male patients with the majority being Malays at 799 (96.9%) patients (Table 4.1).

Table 4.1 Sociodemographic and clinical characteristics of T2DM patients in 2022 Kelantan NDR (n=825).

Variables	n	(%)	Mean	(SD)
Age (years)			55.30	(11.34)
Sex				
Male	292	(35.4)		
Female	533	(64.6)		
Ethnicity				
Malay	799	(96.9)		
Chinese	16	(1.9)		
Others	10	(1.2)		
Smoking Status				
No	775	(93.9)		
Yes	80	(6.1)		
Dyslipidaemia				
No	369	(44.7)		
Yes	456	(55.3)		
BMI (kg/m^2)				
Underweight	24	(2.9)		
Normal	162	(19.6)		
Overweight	348	(42.2)		
Obese	291	(35.2)		
Waist Circumference (cm)				
Normal	326	(39.5)		
Abnormal	499	(60.5)		
HbA1c (%)			8.32	(2.26)
Microalbuminuria				
No	696	(84.4)		
Yes	129	(15.6)		