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SMOKING AS A LIFESTYLE RISK FOR PREHYPERTENSION IN TYPE 2 DIABETES

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ABSTRACT
Type 2 diabetes mellitus and hypertension are lifestyle-related diseases of major public health concern. Preventive strategies have increasingly shifted toward addressing pre-disease stages. Prehypertension, defined as systolic 120–139 mmHg and/or diastolic 80–89 mmHg, is particularly important in T2DM as it increases cardiovascular risk. This study examined the prevalence and associated factors of prehypertension among T2DM patients in Kelantan using 2022 National Diabetes Registry data. Out of 8,657 clinical audit records, 825 non-hypertensive T2DM patients were identified. Prehypertension was present in 73.5% of this group. Logistic regression analysis revealed age (aOR 1.02; 95% CI: 1.003–1.03), female sex (aOR 1.54; 95% CI: 1.10–2.15), and smoking (aOR 2.19; 95% CI: 1.02–4.73) as significant predictors. Although only 6.8% of patients were smokers, smoking more than doubled the risk of prehypertension. In conclusion, prehypertension is highly prevalent among T2DM patients in Kelantan. Both non-modifiable factors (age, sex) and a key modifiable lifestyle factor (smoking) contribute to the increased risk. These findings underscore the need for targeted lifestyle interventions, particularly smoking cessation programs, to prevent progression to hypertension and reduce cardiovascular complications in this vulnerable population.

Keywords: *prehypertension, Type 2 diabetes mellitus, lifestyle, risk factors, smoking*

INTRODUCTION
The global burden of Type II Diabetes Mellitus (T2DM) has escalated dramatically, with prevalence rising from 108 million in 1980 to 422 million in 2014 (WHO, 2023b), making it a leading non-communicable disease (NCD) responsible for a significant portion of global deaths(WHO, 2023a). T2DM rarely presents as a solitary condition, with hypertension being its most common comorbidity. The co-occurrence of T2DM and hypertension profoundly amplifies the risk of cardiovascular morbidity and mortality. Several studies have shown that diabetic patients also diagnosed with hypertension face a 72% increase in all-cause mortality and a 57% increase in cardiovascular disease (CVD) events (G. Chen et al., 2011; Khangura et al., 2018).

In Malaysia, the National Health and Morbidity Survey (NHMS) 2023 documented a prevalence of T2DM at 15.6% and hypertension at 29.2% among adults (National Institutes of Health, 2024). Alarmingly, among T2DM patients specifically, the National Diabetes Registry (NDR) Report 2020 revealed that hypertension prevalence was reported at a

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staggering 80.0% (Ministry of Health, 2021). This high comorbidity underscores the critical need for effective management strategies, as highlighted by the 6th Edition of the Malaysian Clinical Practice Guidelines (CPG) for the Management of Type II Diabetes Mellitus, which clearly outlines the definition and management of hypertension among T2DM patients (Ministry of Health, 2020).

Prehypertension, defined by the Seventh Joint National Committee (JNC 7) as systolic blood pressure between 120–139 mmHg and/or diastolic blood pressure between 80–89 mmHg, serves as a crucial intermediate stage in the progression to overt hypertension (Chobanian et al., 2003). While typically not requiring pharmacological intervention, it is a recognized independent risk factor for cardiovascular disease (Egan & Stevens-Fabry, 2015). For T2DM patients, prehypertension significantly elevates the risk of myocardial infarction, stroke, and overall mortality compared to their normotensive counterparts (Huang et al., 2020; Zhang et al., 2006). Prevalence varies globally: 22–38% in Taiwan, Japan, Korea, and Germany (Erbel et al., 2012; Fukuhara et al., 2012), 52% in Iran (Janghorbani et al., 2008), and up to 45% in Bangladesh (Rahman et al., 2018). In Malaysia, NHMS 2019 estimated a 37% prehypertension prevalence in the general population (National Institutes of Health, 2020).

Despite the established high prevalence of hypertension among T2DM patients and a significant burden of prehypertension in the general population, there remains a notable lack of specific state-level data on the prevalence of prehypertension among T2DM patients in Malaysia, particularly in Kelantan (DOSM, 2024). This data gap is concerning because T2DM patients without a formal hypertension diagnosis might unknowingly be in the prehypertensive range, thereby still being exposed to heightened cardiovascular risks. The importance of preventing progression to full hypertension in T2DM is paramount, especially given that diabetes mellitus has been identified as a strong predictor for prehypertension progression to hypertension. While the Malaysian Clinical Practice Guidelines for T2DM provide comprehensive recommendations for managing established hypertension, their guidance for prehypertensive patients remains limited, largely confined to noting the absence of indication for pharmacological intervention, with little emphasis on tailored lifestyle modification strategies that could delay disease progression. This highlights a crucial area where specific guidance for prehypertension prevention in this high-risk group is lacking.

Various risk factors have been implicated in the development of prehypertension, including sociodemographic, lifestyle and clinical factors including age (H. Ismail et al., 2022), sex (Naidu et al., 2019; Rafan et al., 2018), ethnicity (Chiang et al., 2013), smoking status (Naidu et al., 2019; Song et al., 2018), obesity (Anari et al., 2017; Rahman et al., 2018), dyslipidaemia (H. Ismail et al., 2022), HbA1c level (Abougalambou & Abougalambou, 2013; Chiang et al., 2013) and microalbuminuria (Bianchi et al., 1999).

Among lifestyle factors, smoking has emerged as a particularly important modifiable risk factor. Cigarette smoking contributes to vascular inflammation, endothelial dysfunction, oxidative stress, and heightened sympathetic activation, all of which accelerate the transition from prehypertension to hypertension (Dikalov et al., 2019). Despite extensive guidance on the management of established hypertension in T2DM, relatively little emphasis is placed on smoking cessation as a targeted intervention in the prehypertensive stage. Addressing smoking in T2DM patients with prehypertension is a neglected but essential opportunity to prevent disease progression. Understanding the specific associated factors in the local T2DM population is therefore vital for developing effective interventions.

Therefore, this study aimed to determine the proportion of prehypertension and its associated factors among Type II Diabetes Mellitus patients in Kelantan. By identifying these factors, this research seeks to highlight the burden of prehypertension in this specific population and underscore the importance of devising appropriate, targeted, and tailored

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lifestyle modifications and interventions to prevent its progression to hypertension and reduce associated cardiovascular risks.

METHODS

A cross-sectional study was conducted from December 2023 to June 2024 using Kelantan NDR 2022 data. Out of 8657 registered T2DM patients, 825 fulfilled inclusion criteria of age equal or more than 18 years old, documented as non-hypertensive, and complete records. Exclusion criteria included patients' data with hypertensive-range BP despite non-hypertensive coding, or datasets with >30% missing values.

For sample size determination, the single proportion formula was used to estimate the proportion of prehypertension among T2DM patients, where $Z\alpha$ is 1.96, precision of estimation 0.05 and reported prevalence of prehypertension among T2DM patients in a cohort study was 59.4% (Zhang et al., 2006). The estimated sample size for risk factors association was determined for several variables associated with prehypertension among T2DM patients using Power and Sample Size calculation software. The largest sample size required to answer the study objectives was from sample size for determing proportion of T2DM with prehypertension was 465.

Sampling method: 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.

Research tools and data collection: National Diabetes Registry (NDR) is a web-based data collection system 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. A checklist proforma was designed and used to extract the variables required for this study, which were age, sex, ethnicity, smoking status, waist circumference and body mass index (BMI) (Ministry of Health, 2023b), dyslipidaemia status, systolic blood pressure (SBP), diastolic blood pressure (DBP), HbA1c level, and microalbuminuria. This study used the definition of prehypertension SBP 120–139 mmHg and/or DBP 80–89 mmHg by 7th Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7 Report) (Chobanian et al., 2003).

Statistical analysis: Data were analysed using IBM SPSS v28 software. Descriptive analysis summarised variables. Univariable logistic regression was used to select potential predictors ($p < .25$). Multivariable logistic regression determined adjusted associations. Adjusted odds ratios (aOR) and 95% confidence intervals (CI) were reported. Model adequacy was tested using Hosmer–Lemeshow goodness-of-fit, classification tables, and ROC analysis.

Ethics: Ethical clearance approval was obtained from Universiti Sains Malaysia (JEPeM/KK/23110857) and the National Medical Research Registry (NMRR ID-23-03358-NLF). Written permission was obtained from Director of Kelantan's State Health Department for access and usage of the data following the ethical approval. All researchers involved had declared no conflicts of interest in relation to the study.

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RESULTS

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 analysis. Hence, the final number of patients in this study was 825 patients (Figure 1).

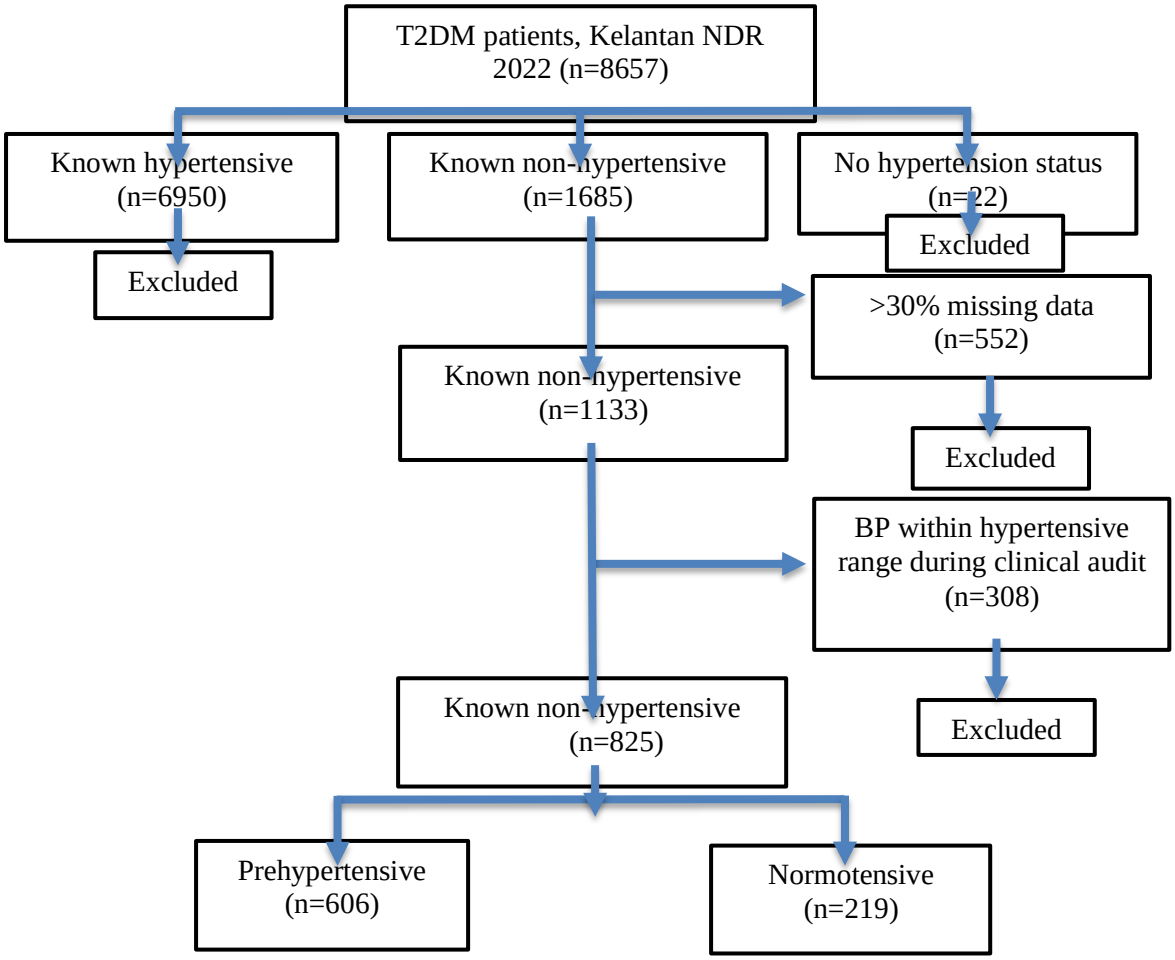

Figure 1: Sample size from total study participants in Kelantan NDR 2022

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 (35.4%) male patients with the majority being Malays at 799 (96.9%) patients (Table 1).

Table 1 Sociodemographic and clinical characteristics of T2DM patients in 2022 Kelantan NDR (n=825).

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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)		

From the 825 patients, 606 (73.5%) patients had blood pressure within prehypertension range, while 219 (26.5%) patients had blood pressure within normotensive range. Simple logistic regression analysis revealed only one significant association which is between the age variable and prehypertension status among T2DM patients (Table 2)

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Variables	Normotension (n=219)				Prehypertension (n=606)				Crude OR (95% CI)	Wald Stat (df)	p-value*
	n	(%)	Mean	(SD)	n	(%)	Mean	(SD)			
Age (year)			53.90	(11.36)			55.81	(11.30)	1.02 (1.003, 1.03)	4.55 (1)	0.033
Sex											
Male	88	(40.2)			204	(33.7)			1		

Table 2 Univariate analysis of associated factors of prehypertension among T2DM patients (n=825)

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Female	131	(59.8)	402	(66.3)	1.32 (0.96, 1.32)	2.98 (1)	0.084
Ethnicity							
Malay	214	(97.7)	585	(96.5)	1		
Non-Malay	4	(1.8)	12	(2.0)	1.10 (0.35, 3.44)	0.03 (1)	0.873
Others	1	(0.5)	9	(1.5)	3.29 (0.41, 26.14)	1.27 (1)	0.260
Smoking Status							
No	210	(95.9)	565	(93.2)	1		
Yes	9	(4.1)	41	(6.8)	1.69 (0.81, 3.54)	1.95 (1)	0.162
Dyslipidaemia							
No	93	(42.5)	276	(45.5)	1		
Yes	126	(57.5)	330	(54.5)	0.88 (0.65, 1.21)	0.62 (1)	0.432
BMI (kg/m^2)							
Underweight	7	(3.2)	17	(2.80)	1		
Normal	42	(19.2)	120	(19.8)	1.18 (0.46, 3.04)	1.11 (1)	0.737
Overweight	94	(42.9)	254	(41.9)	1.11 (0.45, 2.77)	0.05 (1)	0.818
Obese	76	(34.7)	215	(35.5)	1.17 (0.47, 2.92)	0.11 (1)	0.745

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Variables	Normotension (n=219) n (%)	Mean (SD)	Prehypertension (n=606) n (%)	Mean (SD)	Crude OR (95% CI)	Wald Stat (df)	p-value*
Waist Circumference (cm)							
Normal	90 (41.1)		236 (38.9)		1		
Abnormal	129 (58.9)		370 (61.1)		1.10 (0.80, 1.50)	0.31 (1)	0.577
HbA1c (%)		8.35 (2.41)		8.31 (2.21)	0.99 (0.93, 1.06)	0.06 (1)	0.813
Microalbuminuria							
No	177 (80.8)		519 (85.6)		1		
Yes	42 (19.2)		87 (14.4)		0.71 (0.47, 1.06)	2.82 (1)	0.093

Table 2 Continued

*Simple logistic regression

Multiple logistic regression analysis revealed the significant adjusted associated factors of prehypertension among T2DM patients were age, sex and smoking status when other variables were controlled (Table 3).

Table 3 Associated risk factors of prehypertension among diabetic patients (n=825)

Variables	B	Wald Stat (df)	Adjusted OR (95% CI)	*p*-value*
Age	0.02	6.17 (1)	1.02 (1.003, 1.03)	0.012
Sex				
Male			1	
Female	0.43	6.25 (1)	1.54 (1.10, 2.15)	0.013
Smoking				
No			1	
Yes	0.79	4.00 (1)	2.19 (1.02, 4.73)	0.045

*Multiple logistic regression
Constant -0.968
Method Enter was applied.
No multicollinearity and interactions.
Hosmer Lemeshow test, *p*-value 0.136
Classification table 73.3% correctly classified
Area under Receiver Operating Characteristics (ROC) curve 59.2%

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For every one-year increase in age, T2DM patients have 1.018 odds of developing prehypertension (aOR 1.02; 95% CI: 1.003, 1.03; p = 0.012) when other variables were controlled. Female T2DM patients have 1.54 odds of developing prehypertension compared to males (aOR 1.54; 95% CI: 1.10, 2.15; p = 0.013) when other variables were controlled. Smoking diabetic patients have 2.19 odds of developing prehypertension compared to non-smoking diabetic patients (aOR 2.19; 95% CI: 1.02, 4.73; p = 0.045) when other variables were controlled.

DISCUSSION

This study revealed slightly different findings in terms of sociodemographic characteristics of the diabetic patients compared to findings from National Diabetes Registry (NDR) Report 2020 (Ministry of Health, 2021). The mean (SD) age of the diabetic patients in this study was 55.3 (11.34) years old, which is slightly higher than the reported mean age of diabetic patients at 53 years old in the report. Consistent with the NDR Report showing a higher prevalence of diabetes among women, this study also found a greater proportion of female patients; however, the percentage observed (64.6%) was notably higher than the 57.0% reported in the report. This is also quite disproportionate to the comparable distribution of 41% female and 59% male population in Kelantan (DOSM, 2024). This finding matches the well-known findings on sex difference in health seeking behaviours where more women were shown to tend to seek health intervention and promotion activities at a younger age than men (Thompson et al., 2016). The ethnicity makeup of the study sample was predominated by Malay ethnic at 96.9% which is substantially higher than the reported 59.4% in the NDR report; this disparity, however, correctly reflects and could be attributed to the 95.9% of Kelantan population being Malays (DOSM, 2024).

This study found that 6950 (80.3%) of the diabetic patients were hypertensive which is almost equal to the reported 80.0% prevalence of hypertension among diabetic patient in NDR Report 2020 (Ministry of Health, 2021). The prevalence of hypertension among T2DM population is much higher in comparison to the latest hypertension prevalence among general population at 29.2% (National Institutes of Health, 2024) suggesting the higher risk of hypertension for T2DM population. This further signifies the burden of multiple comorbidities of diabetes and hypertension among the T2DM population and subsequently the increased risks in cardiovascular morbidity and mortality in this already high-risk population.

Among those who did not have a hypertension diagnosis, 27.2% were noted to have hypertensive range systolic blood pressure and/or diastolic blood pressure reading during the clinical audit. These patients were categorized as undiagnosed hypertension in this study. National Health Morbidity Survey 2019 survey reported a 14.1% national prevalence of undiagnosed hypertension among the general population with large variation observed across the states: Kelantan having the highest prevalence at 21.4% (National Institutes of Health, 2020). Thus, not only that T2DM patients have higher prevalence of hypertension, but this study was also able to demonstrate the higher prevalence of undiagnosed hypertension among the T2DM patients compared to the general population.

After excluding the undiagnosed hypertensive T2DM patients, the prevalence of prehypertension among the remaining non-hypertensive patients was 73.5%. This figure was significantly higher than the prevalence of prehypertension among diabetic patients reported in United States of America at 59.4% (Zhang et al., 2006). However, many other studies focuses on the prevalence of prehypertension among general population only which ranged from 21% in China (Yu et al., 2008), 37.7% in Japan (Fukuhara et al., 2012), 26.2% in Germany (Erbel et al., 2012), and 52.1% in Iran (Janghorbani et al., 2008). A recently published baseline findings of the Prospective Urban Rural Epidemiology (PURE) Malaysia Cohort Study carried out among 7585 adults revealed prehypertension prevalence in the general population at 40% (R. Ismail et al., 2023). It is important to remember that the

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alarmingly higher prevalence in the current study could be attributed to the sample population in this study which comprised of only T2DM patients from the clinical audit datasets in 2022 Kelantan NDR in comparison to other studies which either also included non-diabetic individuals or involving general population.

Normotensive diabetic patients made up the remaining 26.5% of the study participants. Not only the prevalence of established hypertension and undiagnosed hypertension were high among T2DM patients in Kelantan, the prevalence of prehypertension was also more than double of the normotension prevalence. The undiagnosed hypertensive T2DM patients and those who were unknowingly within prehypertension range represented the T2DM populations who were exposed to increased cardiovascular risks, but lacking interventions given to them for prevention of cardiovascular morbidity and mortality as well as prevention from progression into hypertension, respectively.

The rate of progression from prehypertension to hypertension among the general population reported in a prospective cohort study of over 11.8 years duration involving 12,490 participants in Japan was 26.1% (Ishikawa et al., 2017). This study also demonstrated 2.95 times increased risk of cardiovascular diseases (CVD) among those who progressed to hypertension. Using the figure as reference, at least more than a quarter of the prehypertensive T2DM patients (158 patients) in this study would be progressing into full hypertensive and thus being subjected to even higher risks of CVD.

Complex pathophysiological mechanisms in T2DM pathophysiology coincide with the development of hypertension as its comorbidity. Among the mechanisms, the most discussed mechanism is insulin resistance state which leads to activation other mechanisms including inappropriate activation of sympathetic nervous system, SNS, and excitatory effects on the renin-angiotensin-aldosterone system (RAAS) (Ferrannini & Cushman, 2012). These mechanisms interact with multiple associated factors and contribute further to the development of hypertension as well as cardiovascular diseases (Galicia-Garcia et al., 2020). Prehypertension, which is a state where an individual systolic blood pressure ranges 120 - 139 mmHg and/or diastolic BP ranges 80 – 89 mmHg (Chobanian et al., 2003), faces similar pathophysiological process before progressing into full hypertension, should no intervention was implemented.

Age

Three significant associated factors of prehypertension among T2DM patients in Kelantan were determined in the current study. The first two were non-modifiable sociodemographic factors age and sex. A non-hypertensive T2DM patient in this study experienced a small but significant odd (aOR 1.02; 95% CI: 1.003, 1.03; p = 0.012) of developing prehypertension with each passing year. Age is a significant associated factor for both prehypertension and hypertension regardless of diabetes mellitus status. As an individual ages, the decreasing arterial compliance of the blood vessels, and thickening and hardening of the atherosclerotic plaque, especially in the region of carotid sinus resulting in reduced baroreceptor sensitivity, lead to an increased in blood pressure reading (Weber et al., 1989). However, for T2DM patients, the mechanism of insulin resistance states further affects this arterial stiffening which promotes development of prehypertension and subsequently hypertension among T2DM patients (Koenen et al., 2021) compared to non-diabetic individuals. Atherosclerosis Risk in Community (ARIC) Study was able to demonstrate this through their findings of all indexes of arterial stiffness increase with higher concentration of fasting glucose in T2DM patients (Salomaa et al., 1995). The inappropriate activation of the renin-angiotensin-aldosterone system, RAAS (Miller et al., 1996) and sympathetic nervous system, SNS (Muntzel et al., 1995) in the states of insulin resistance also resulted in increased vascular resistance. The decline in the peripheral vascular β-receptors activity with age likely also explained the dysregulation in the RAAS and SNS (Weber et al., 1989). Insulin resistance state also causes upregulation of the

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sodium-glucose cotransporter 2 (SGLT 2) which then results in increased glucose and sodium absorption at the proximal tubule of the kidney (Aroor et al., 2018). This contributes to increased intravascular volume which then, compounded by other effects of insulin resistance described, leads to prehypertension and subsequently hypertension.

Sex

The second non-modifiable sociodemographic factor significantly associated with prehypertension in the current study was sex. A female non-hypertensive T2DM patient in this study has 1.536 odds (aOR 1.54; 95% CI: 1.10, 2.15; p = 0.013) of developing prehypertension compared to male T2DM patient. This finding contrasts with the higher prehypertension prevalence among males found during literature review (Naidu et al., 2019; Rafan et al., 2018; Rahman et al., 2018). However, this contrasting finding is not a unique occurrence. It was found that the different sex experienced different pattern of risk factor for diseases at different stages of life therefore any intervention and strategies in prevention of prehypertension from progressing into full hypertension to be tailored accordingly to each sex (Kim & Lee, 2015). Moreover, Kautzky-Willer et al. (2016) further reiterated the differences in predisposition for development of diseases between men and women, namely biological differences, lifestyle practices including physical activities and high risk behaviour such as smoking and alcohol consumption, culture and socioeconomic status (Kautzky-Willer et al., 2016). The current study was able to demonstrate female T2DM patients having higher odds of developing prehypertension likely attributed to the large discrepancy in the sample population where the number of female patients (64.6%) almost double that of male patients (35.4%). The difference in health seeking behaviours where women exhibits more tendencies for health screening and intervention might also contributed to this finding (Thompson et al., 2016).

Smoking status

While age and female sex were identified as significant non-modifiable factors, smoking emerged as the sole significant modifiable lifestyle risk factor, more than doubling the odds of prehypertension (aOR 2.19; 95% CI: 1.02, 4.73; p = 0.045). Despite only 6.1% of patients being current smokers, this association underscores the powerful impact of tobacco use in amplifying vascular risk within an already vulnerable diabetic population.

The biological plausibility of this finding is well established. Smoking induces sympathetic nervous system activation, increases arterial stiffness, promotes oxidative stress, and impairs nitric oxide–mediated vasodilation (Kopp, 2022). In T2DM patients, these effects act synergistically with insulin resistance and chronic low-grade inflammation, accelerating endothelial dysfunction and vascular remodeling (Galicia-Garcia et al., 2020). Nicotine also potentiates activation of the renin-angiotensin-aldosterone system, further contributing to elevated blood pressure (Oakes et al., 2018). Collectively, these mechanisms explain why smoking substantially increases the risk of progression from prehypertension to hypertension in diabetic individuals.

Beyond its isolated effect, smoking interacts with other lifestyle factors to magnify cardiovascular risk. Evidence from cohort studies shows that the coexistence of smoking with poor diet, sedentary behavior, and excessive alcohol consumption markedly increases the incidence of hypertension and related complications compared with any single factor alone (Du et al., 2024). This clustering of unhealthy behaviors is particularly relevant in populations with T2DM, who already face elevated baseline cardiovascular risk. Thus, smoking not only directly accelerates progression from prehypertension to hypertension but also compounds the detrimental impact of other lifestyle risks.

There were conflicting findings on smoking status association with prehypertension. Song et al. (2018), Naing and Aung (2014) and Liu et al. (2018) found that smoking is significantly associated with prehypertension. On the other hand, Ismail et al. (2022) and Rafan et al. (2018) did not find similar association in their study. Controversially, Okubo et al. (2002) in their study even reported a lower range of blood pressure among smokers

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compared to non- and ex-smoker. Although previous studies on smoking and prehypertension have reported mixed results, smoking regardless still proves to be one of the leading modifiable risk factors of death and disability worldwide (IHME, 2024). In Asian populations, smoking has been shown to contribute disproportionately to cardiovascular events among individuals with metabolic disorders, including T2DM (Gu et al., 2009). Our study therefore reinforces the need to view smoking not only as a critical accelerator of prehypertension progression in T2DM but also as a general cardiovascular hazard. Despite the small number of smokers among the T2DM patients in this study, a significant association could still be elicited suggesting the strong association of smoking and prehypertension among the study sample. As such, smoking cessation as per recommended in WHO Package of Essential Noncommunicable (PEN) Disease Interventions for Primary Health Care must be prioritized and encouraged to all T2DM patients in this study (WHO, 2020). While age and sex are non-modifiable, smoking is highly amenable to intervention. However, in Malaysia, cessation programs are often underutilized, and integration into diabetes care pathways remains limited. Existing initiatives such as KOSPEN and Quit Smoking Clinics should be expanded and more tightly integrated into diabetes management programs.

Other associated factors studied were not found to be significantly associated with prehypertension among the T2DM patients in the current study. These factors were ethnicity, dyslipidaemia, BMI, waist circumference, HbA1c level and microalbuminuria.

In Malaysia, Malay ethnicity was reported to have a significant association with prehypertension in a study by Mahadir Naidu et al. (2019) while Chinese ethnicity was reported in a study by Ismail et al. (2022). Song et al. (2018) on the other hand reported no significant differences on prehypertension prevalence among the three main ethnicities Malay, Chinese, and Indian in the neighbouring country Singapore. NDR Report 2020 did report Malay as the ethnic with highest hypertension prevalence among the diabetic patients, however, no data was published on prehypertension prevalence (Ministry of Health, 2021). It is possible that there was an ethnicity with predominance for prehypertension among the T2DM population however, in the current study in Kelantan, ethnicity was not found to be significantly associated with prehypertension due to the Malays comprising 96.9% of the sample population.

BMI and waist circumference are two factors that are closely related to prehypertension in T2DM populations. General obesity examined through BMI classification and central obesity which was measured in the current study by waist circumference were both associated with prehypertension among both diabetic and non-diabetic patients. Visceral fats released proinflammatory adipokines leptin and aldosterone that worsen vascular insulin resistance and trigger systemic inflammatory response (Huby et al., 2015). The proinflammatory cytokines also impair vascular relaxation resulting in further vascular stiffness and subsequent development of prehypertension (Reddy & Natarajan, 2011). These inflammatory processes also cause vascular inflammation and endothelial dysfunction which further exacerbates progression of prehypertension to hypertension (Guarner & Rubio-Ruiz, 2015). Mamdouh et al. (2022) found that overweight and obese populations had a higher prevalence of prehypertension in their study among adults in Dubai. In the current study, the percentage of each BMI category was comparable in both prehypertensive and normotensive T2DM patients. Similar findings were also observed for the high percentage of abnormal waist circumference in both prehypertensive (61.1%) and normotensive (58.9%) T2DM patients. This might explain why BMI and waist circumference were not found to be associated with prehypertension among the T2DM patients. Nevertheless, higher BMI and abnormal waist circumference are known and well-established risks of CVD, especially among T2DM populations. This findings highlight the need for more intensive general and central obesity management among the T2DM populations in Kelantan.

In Malaysia 6th Edition CPG Management of Dyslipidaemia 2023, dyslipidaemia was defined as total cholesterol (TC) level > 5.2 mmol/l, or high-density lipoprotein cholesterol

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HDL-C level < 1.0 mmol/l for male patients and < 1.2 mmol/l for female patients or triglyceride (TG) level > 1.7 mmol/l and low-density lipoprotein cholesterol while LDL-C level depends on individual patient's cardiovascular risks (Ministry of Health, 2023a). Erina et al. (2017) found in their study that was adjusted for sex, age and obesity, dyslipidaemia was significantly associated with prehypertension with hypercholesterolemia level > 4.9mmol/l (aOR 1.27, 95% CI: 1.15, 1.39), increased HDL level > 3.0 mmol/l (aOR 1.25, 95% CI: 1.14, 1.37) and triglyceride level > 1.7 mmol/l (aOR 1.39, 95% CI: 1.23, 1.58). Recently, there was an increase in the use of triglyceride-glucose (TyG) index in determining the risks of cardiovascular morbidity and mortality (Lopez-Jaramillo et al., 2023). Xie et al. (2021) was able to demonstrate that TyG index was associated with higher rate of prehypertension as well as outperforming fasting plasma glucose (FPG) at discerning prehypertension risk. In a recent population based retrospective study on prehypertension and hypertension among east Asia populations, Chen et al. (2023), explored further and found that triglyceride glucose-BMI index (TyG-BMI) to exhibit excellent prediction power for prevalence of prehypertension and hypertension across all Japanese and Chinese populations in the study. In this current study however, only dyslipidaemia status was used as the variable thus the actual values of lipid parameters were not able to be explored. Even though dyslipidaemia was not reported to be a significant associated factor in this study, the increased in CVD risks due to dyslipidaemia is indisputable (Gonna & Ray, 2019). In current study, the percentage of dyslipidaemia status among the whole T2DM patients and percentage of dyslipidaemia among prehypertensive T2DM patients were almost similar at 55.3% and 54.5% respectively, signifying that a high number of the T2DM patients were subjected to increased risks of CVD from dyslipidaemia. Therefore, these patients would benefit from further studies exploring the utility of advanced lipid indices to improve early risk stratification and intervention strategies.

HbA1c had been reported to be associated with increased prevalence of hypertension and increased risk of CVD (aOR 1.39; 95% CI: 1.06, 1.83) with every 1% increment of HbA1c level among the original cohort of the Framingham study (Singer et al., 1992). A more recent study Heo and Ryu (2018) was also able to demonstrate a similar significant association between HbA1c level with both hypertension and prehypertension prevalence. The HbA1c levels target recommended by Clinical Practice Guidelines: Management of Type II Diabetes Mellitus 2020 is tailored to individual patients (Ministry of Health, 2020). Newly diagnosed, younger and healthier patients with low risk of hypoglycaemia and no microalbuminuria are recommended to keep a tight control on HbA1c level of less than or equal to 6.5% while elderly patients with multiple comorbidities and at risk of hypoglycaemia and fall are to maintain less tight control on HbA1c level between 7.1% to 8.0%. HbA1c level ranging from 6.6% to 7.0% is recommended for other T2DM patients who do not fall within either of the groups. The mean (SD) HbA1c levels among prehypertensive T2DM patients and normotensive T2DM patients in this study were almost equal at 8.31% (2.21) and 8.35% (2.41) respectively. Even if the majority of the T2DM patients belong within the less tight control of HbA1c level (between 7.1% to 8.0%.), their HbA1c levels still exceeded the recommended target by CPG T2DM. This equal distribution might have contributed to HbA1c level not being a significant associated factor for prehypertension among the T2DM patients in this study. Nonetheless, efforts should be made to address and improve the glycaemic control of these patients.

Microalbuminuria was not found to be significantly associated with prehypertension among the T2DM patients in this study. The small number of T2DM patients having microalbuminuria might have contributed to this finding. Microalbuminuria was demonstrated in diabetic patients with higher insulin resistance state and these patients were found to have thicker carotid arteries. This predisposed these patients to higher risk of prehypertension and subsequent hypertension (Bianchi et al., 1999). Another study found that microalbuminuria could even be an independent and strong predictor of CVD irrespective of diabetes and hypertension diagnosis (Klausen et al., 2004). Even though a

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significant association was not observed between microalbuminuria and prehypertension in the current study, it was still a worthwhile endeavor to determine this predisposition among the T2DM populations in Kelantan. In short, these factors were not significantly associated with prehypertension in our cohort, likely due to the uniformly high prevalence across both normotensive and prehypertensive groups.

This study has found a considerably high proportion of prehypertension among the non-hypertensive T2DM patients in Kelantan. Both similar and contrasting findings with available literature were demonstrated in this study. Albeit by small odds, increasing age, female sex and smoking status were statistically significantly associated with prehypertension among T2DM patients while their ethnicity, dyslipidaemia status, BMI, waist circumference measurement, HbA1c level and presence of microalbuminuria bore no significant association.

Managing prehypertension in patients with T2DM is a critical consideration due to the heightened risk of cardiovascular events. The current approach, largely guided by the JNC 7, emphasizes non-pharmacological interventions over drug therapy (Chobanian et al., 2003). These lifestyle modifications were outlined in both CPG T2DM (Ministry of Health, 2020) as well as 5th Edition CGP for Hypertension (Ministry of Health, 2018) under the management of T2DM and hypertension respectively. Unlike prediabetes with its own section in CPG T2DM, prehypertension, however, was not discussed under its own specific section in any of the CPGs. This strategy focuses on lifestyle modifications, which have been shown to be effective in preventing the progression of prehypertension to full-blown hypertension and reducing overall cardiovascular risk.

A cornerstone of this approach is the Dietary Approaches to Stop Hypertension (DASH) diet of high intake of fruits, vegetables, and low-fat dairy while limiting red meat, refined carbohydrates, and saturated fats (Appel et al., 2006). A meta-analysis confirmed that the DASH diet not only significantly lowers blood pressure but also improves cholesterol levels (Siervo et al., 2015). Beyond diet, physical activity is a vital component. For most T2DM patients, recommended activity includes at least 150 minutes per week of moderate-intensity aerobic exercise or 75 minutes of vigorous activity, supplemented by resistance training at least twice a week (Ministry of Health, 2020). Several studies have provided strong evidence that various forms of exercise effectively reduce blood pressure in both hypertensive and prehypertensive populations (Börjesson et al., 2016; Pescatello et al., 2019). Other key lifestyle changes include weight loss, where each kilogram of body weight reduction can lower blood pressure by approximately 1 mmHg (Neter et al., 2003), and smoking cessation, which has been shown to reduce blood pressure without negatively impacting glycemic control in diabetic patients (Hieshima et al., 2018). These non-pharmacological strategies are well-established and are incorporated into national clinical practice guidelines.

The use of pharmacological agents for prehypertension remains a subject of considerable debate, primarily due to conflicting trial evidence. The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial raised concerns by finding that intensive blood pressure control (below 120 mmHg) in diabetic patients was linked to a higher incidence of adverse cardiovascular events (Mancia, 2010), a phenomenon known as the "J-shape phenomenon" (ACCORD Study Group et al., 2010; Fuchs & Fuchs, 2014). Conversely, other major trials presented a more nuanced picture. The Perindopril Protection Against Recurrent Stroke Study (PROGRESS) trial demonstrated that lowering systolic blood pressure to below 120 mmHg progressively reduced the risk of recurrent hemorrhagic stroke (Arima et al., 2006). However, studies like International Verapamil-Trandolapril Study (INVEST) and Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET) suggested that while blood pressure reduction might be cerebroprotective against stroke, it could also increase the risk of coronary events (Messerli et al., 2006; Sleight et al., 2009). These findings highlight the delicate balance between risks and benefits when considering drug therapy for prehypertension.

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Given this conflicting evidence, national guidelines have not yet endorsed pharmacological treatments for prehypertension. The current consensus remains focused on robust lifestyle modification interventions. Nonetheless, this underscores the importance of increasing awareness of prehypertension among both healthcare practitioners and T2DM patients. This heightened vigilance is crucial for early detection and effective management, particularly since the combination of prehypertension and T2DM significantly increases the risk of cardiovascular morbidity and mortality (Khosravi et al., 2017). While diet, physical activity, and weight reduction remain important for overall risk reduction, the unique and independent contribution of smoking in our findings highlights a gap in current practice and policy that should be urgently addressed.

Limited literature on prehypertension in T2DM shifts discussion toward studies on hypertension in T2DM and prehypertension in the general population. Nonetheless, this highlights opportunities for future research and the need to consider tailored management approaches for prehypertension in diabetic patients.

This study is the first to report the burden of prehypertension among T2DM patients in Kelantan, providing evidence to guide interventions and future research. The cross-sectional design using secondary data was cost-effective and strengthened by logistic regression analysis.

However, limitations must be acknowledged. Secondary data use introduced potential information bias from varied devices and single blood pressure readings. The cross-sectional design prevented causal inference, and the limited NDR variables restricted exploration of other potential determinants such as education, family history, diet, and physical activity. Odds ratios close to one and modest model fitness also suggest analytical constraints. Lastly, findings based solely on Kelantan data from 2022 may not be generalizable to other populations or time periods.

CONCLUSION

The study revealed a high prevalence of prehypertension among T2DM patients in Kelantan. The findings identified several significant associated factors for prehypertension among T2DM in Kelantan which were age, sex, and smoking. Smoking emerged as the only significantly associated modifiable risk factor which underscores the crucial need for lifestyle modification and importance of enhancing smoking cessation promotions and programs among T2DM patients to prevent the development of prehypertension.

Recommendation and future research. The management of T2DM should incorporate prehypertension as a priority to ensure early identification and intervention, reducing overall cardiovascular risk in this vulnerable group. Greater awareness is needed among healthcare providers and patients regarding the risks of prehypertension in T2DM, supported by professional training, patient education, and effective communication. Future research should explore longitudinal outcomes to confirm the causal role of smoking in progression from prehypertension to hypertension among T2DM patients. Policymakers and healthcare providers must recognize that tackling smoking in this population is not only a matter of general tobacco control but an essential step in preventing the escalation of cardiovascular risk in diabetes care.

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