PREVALENCE AND RISK FACTORS FOR DYSLIPIDEMIA AND HYPERTENSION IN DIABETES MELLITUS AMONG THE PAEDIATRIC POPULATION IN HOSPITAL UNIVERSITI SAINS MALAYSIA (USM), KELANTAN, MALAYSIA

DR MOHAMAD QAZREEN BIN AHMAD SHAWALUDIN

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT

FOR THE DEGREE OF MASTER IN MEDICINE

(PAEDIATRICS)

UNIVERSITI SAINS MALAYSIA

2023

Principal Investigator:

Dr. Mohamad Qazreen AHMAD SHAWALUDIN

Department Paediatric, School of Medical Sciences,

Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan

Main supervisor:

Dr. Suhaimi HUSSAIN

Consultant Paediatric Endocrinologist,

Department of Paediatric, School of Medicine Sciences,

Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan

Co-supervisor:

Dr.Najib Majdi YAACOB

Medical Lecturer/ Public Health Specialist

Department of Biostatistics and Research Methodology, School of Medical Science,

Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan

Acknowledgment

In the name of Allah, the most gracious and most merciful. I am thankful to ALMIGHTY ALLAH for all the strength, trials, and opportunities showered on me to complete my thesis within a given time. Undertaking this post-graduate thesis has been a life-changing experience, and it would not have been possible without support and guidance from people's surroundings.

First and foremost, I sincerely thank my respected supervisor Dr. Suhaimi bin Hussain for his expertise, assistance, and guidance while conducting this study. Most importantly, he has provided positive encouragement, support, and a warm spirit to complete this thesis. With his guidance and constant feedback, this thesis was achievable. I am also thankful to my co-supervisor, Dr. Najib Majdi, for their advice and contribution to this thesis.

I humbly extend my special thanks to my fellow lecturers, colleagues, staff members of Hospital Universiti Sains Malaysia (USM), family, and friends for their encouragement and supports along the walks. May this work benefit others.

TABLE OF CONTENTS

LIST OF TABLES AND FIGURES

LIST OF ABBREBIATION AND NOMENCLATURE

USM	:	Universiti Sains Malaysia
DM	:	Diabetes Mellitus
DM1	:	Diabetes Mellitus Type 1
DM2	:	Diabetes Mellitus Type 2
BMI	:	Body Mass Index
SMBG	:	Self-Monitoring Blood Glucose
HbA1c	:	Haemoglobin A1c
BP	:	Blood Pressure
LDL	:	Low-Density Lipoprotein
HDL	:	High-Density Lipoprotein
TG	:	Triglyceride
TC	:	Total Cholesterol
OR	:	Odd Ratio
CI	:	Confidence Interval
SD	:	Standard Deviation
IQR	:	Interquartile Range

ABSTRAK

Kelaziman dan Faktor – Faktor Risiko berkaitan Masalah Darah Tinggi dan Dislipidemia bagi Penyakit Kencing Manis dalam kalangan Kanak- Kanak di Hospital Universiti Sains Malaysia (USM), Kelantan, Malaysia.

Objektif:

Kajian adalah bertujuan menilai kelaziman dan faktor-faktor risiko masalah darah tinggi dan dislipidemia bagi penyakit kencing manis dalam kalangan kanak- kanak di Hospital Universiti Sains Malaysia (USM), Kelantan, Malaysia.

Kaedah:

Kajian secara retrospektif telah dijalankan di Hospital Universiti Sains Malaysia (USM), Kelantan, Malaysia. Seramai 132 pesakit yang mengidap penyakit kencing manis sekurang –kurangnya 6 bulan, berumur di bawah 18 tahun the menyertai kajian ini. Data demografik (umur, pendapatan ibu bapa, sejarah keluarga, tinggi, berat, indek jisim badan dan tekanan darah), sejarah klinikal kencing manis (jenis kencing manis, tempoh, umur mengidap, pemantauan SMBG dan jenis rawatan) dan maklumat makmal (HbA1c, profil lemak) telah diperolehi dari rekod perubatan pesakit. Kaedah "Multiple Logistic Regression" model telah digunakan untuk memeriksa hubungan antara pelbagai risiko untuk darah tinggi dan dislipidemia dalam kalangan kanak –kanak penyakit kencing manis.

Keputusan:

Sejumlah 132 pesakit telah dikaji, sebanyak 53.8% adalah perempuan dengan median umur 16.0 (13.0 – 17.0) tahun dan median umur mengidap penyakit kencing manis 10.0 (8.0 – 12.0). Kajian menunjukan kelaziman masalah dislipidemia dan darah tinggi sebanyak 62.1%

dan 19.7%. Analisis berdasarkan “multiple logistic regression” menunjukan tekanan darah sistolik (adjusted OR, 95% Cl) 1.07 (1.02,1.12),tempoh penyakit kencing manis (tahun) 1.76 (1.37,2.25), bacaan HbA1c (1.06,1.72) adalah faktor yang bermakna untuk dislipidemia, manakala berat (kg) 1.16 (1.07,1.25),tempoh kencing manis (tahun) 1.49 (1.14,1.96), nilai HbA1c (%)1.56 (1.12,2.15) dan nilai LDL (mmol/L) 2.98 (1.11,7.95) faktor bermakna untuk tekanan darah tinggi dalam kalangan kanak – kanak kencing manis.

Kesimpulan:

Kelaziman untuk dislipidemia dan tekanan darah tinggi bagi penyakit kencing manis dalam kalangan kanak – kanak di pusat kajian ini adalah 62.1% dan 19.7%. Faktor - faktor yang sangat bermakna bagi dislipidemia dan tekanan darah tinggi dalam kajian ini adalah tempoh mengidap penyakit kencing manis dan kawalan glisemik HbA1c.

Kata Kunci: Dislipidemia, tekanan darah tinggi, penyakit kencing manis kanak-kanak, faktor-faktor risiko.

(Jumlah: 283 perkataan)

ABSTRACT

Prevalence and Risk Factors for Dyslipidemia and Hypertension in Diabetes Mellitus among the Paediatric Population in Hospital Universiti Sains Malaysia (USM), Kelantan, Malaysia

Objective:

This study aims to evaluate the prevalence and risk factors for dyslipidaemia and hypertension in diabetes mellitus among the pediatric population in Hospital Universiti Sains Malaysia (USM), Kelantan, Malaysia

Method:

A retrospective cross-sectional study was conducted at Hospital Universiti Sains Malaysia (USM), Kelantan, Malaysia. A total of 132 patients diagnosed with diabetes mellitus for at least six months, aged below 18 years old, were recruited for this study. Demographic data (age, race, parent's monthly income, family history of cardiovascular disease, height, weight, body mass index (BMI), and blood pressure), diabetes profile (type and duration diabetes, age of diagnosis, SMBG monitoring, and type of treatment) and laboratory values (HbA1c, lipid profile) were obtained from patient's medical records. Multiple logistic regression models were used to examine the associations between risk variables with dyslipidemia and hypertension in diabetes mellitus children.

Result:

A total of 132 patients were studied, 53.8% female, with a median age of 16.0 (13.0 – 17.0) years and an age of diagnosis of 10.0 (8.0 -12.0) years. We found that the prevalence of dyslipidemia and hypertension was 62.1% and 19.7%, respectively. Multiple logistic regression analysis showed systolic blood pressure (mmHg) (adjusted OR, 95% CI) 1.07 (1.02, 1.12), diabetes duration (years) 1.76 (1.37, 2.25), and HbA1c value 1.35 (1.06, 1.72) were the

significant prognostic factors for dyslipidaemia. Meanwhile, weight (kg) 1.16 (1.07,1.25), duration of diabetes (years) 1.49 (1.14, 1.96), HbA1c (%) 1.56 (1.12, 2.15) and LDL value (mmol/L) 2.98 are significant factors for hypertension.

Conclusion:

The prevalence rates of dyslipidaemia and hypertension in pediatric diabetes mellitus referred to our center were 62.1% and 19.7%, respectively. The most significant prognostic factors for dyslipidaemia and hypertension were the duration of diabetes and glycaemic control (HbA1c).

Keywords: dyslipidaemia, hypertension, pediatric diabetes mellitus, risk factors

(Total: 281 words)

CHAPTER II

THE TEXT

2.1

Section A

Introduction

INTRODUCTION:

Diabetes mellitus is the most common metabolic and endocrine disorder worldwide, with a global prevalence in 2019 estimated to be 9.3% (1). Based on the World Health Organization (WHO), the number of people with diabetes rose from 108 million in 1980 to 422 million in 2014 (2). Among Asian countries, the prevalence of DM increased to 10.3% in 2021, which contributing more than 60% of diabetic's world population (3). Meanwhile, in Malaysia, the prevalence of diabetes mellitus up to 14.39% especially in pre diabetes and type 2 diabetes (4). It is a complex disorder characterized by elevated blood glucose levels resulting from defective insulin secretion, resistance, or both (5). The etiology of diabetes mellitus is heterogeneous. Most cases are classified into two major pathophysiological categories: type 1 diabetes and type 2 diabetes. Type 1 diabetes mellitus (DM1) is a condition characterized by absolute insulin deficiency, which can be detected using genetic and pancreatic islet autoimmunity markers. In contrast, type 2 diabetes mellitus (DM2), is a combination of insulin resistance with a relative insufficiency of compensatory insulin secretion responses (5)

The incidence of DM1, which accounts for 90% of cases, occurs in children typically manifest between the ages of four and six years or between 10 and 14 years. In comparison, DM2 increases in older children parallel to childhood obesity, with the highest rate between the ages of 14 and 19 years old (6). Many long-term complications are associated with poorly controlled diabetes mellitus. These complications presented after a few years of diabetes mellitus onset resulting from oxidative stress, inflammation, and hypercoagulability process, leading to endothelial injury and silent atherosclerosis changes (7,8). According to Brazilian study, high blood pressure and dyslipidaemia, are

the most serious cardiovascular complications, causing poor quality of life and reducing life expectancy by 10-20 years (8)

Based on several worldwide studies, the prevalence of dyslipidaemia ranges from 3% to 75%, while hypertension in pediatric diabetes mellitus is up to 23%, depending on other risk factors (9,10). A recent study in 2019 from Lithuania showed the prevalence of dyslipidaemia and hypertension in children with diabetes mellitus was 29.8% and 62.6%, respectively (11). A study by Thais KH et al. reported the prevalence of dyslipidaemia was 72%, predominantly in females, pubertal age, and the overweight group (8). According to local Diabetes in Children and Adolescents Registry (Di CARE), 2006-2008 data, Ministry of Health (MOH) the prevalence of dyslipidaemia is 5% in DM1 and 16% in DM2 (12).

The SEARCH study reported a high prevalence of hypertension: 23.7% in DM2 and 5.9% in DM1. The study revealed obesity and poor glycaemic control were each associated with high blood pressure (13). While people with suboptimal glycaemic control has higher lipid abnormalities resulting in higher prevalence of dyslipidaemia (13). A large multicentre study from Brazil by Marilia B. Gomes et al. showed the prevalence of hypertension in DM1 children and adolescents was 8.3%, indicating a four-fold higher risk in obese and overweight groups (14). Most studies reported that diabetes duration, obesity, and HbA1c were the most significant prognostic factors for dyslipidaemia and hypertension in pediatric diabetes mellitus (11,15)

Despite the increasing prevalence of dyslipidaemia and hypertension in pediatric diabetes mellitus worldwide, there are limited studies have been conducted in Malaysia. The only data that is available for pediatric diabetes mellitus is Di CARE 2008, which

not a true representative of our national data since most of the subjects were recruited from Klang Valley only. Therefore, the purpose of this study is to determine the prevalence and significant prognostic factors for dyslipidemia and hypertension in children with diabetes mellitus. Furthermore, the study's findings will be added not only to local data bases, but also to international paediatric hypertension and dyslipidaemia research.

2.2

Section B

Study Protocol

2.2.1

Documents submitted

for Ethical Approval

DR MOHAMAD QAZREEN BIN AHMAD SHAWALUDIN

UNIVERSITI SAINS MALAYSIA

2020

Research Title

Prevalence and Risk Factors for Hypertension and Dyslipidemia in Diabetes Mellitus among Paediatric Population in Hospital Universiti Sains Malaysia (USM), Kelantan.

Researcher:

Dr. Mohamad Qazreen Bin Ahmad Shawaludin (MMC:69580)

Paediatric Medical Officer and Post Graduate student.

Paediatric Department, Hospital Universiti Sains Malaysia (USM)

Supervisor:

Dr. Suhaimi Bin Hussain, Consultant Paediatrician

Endocrinologist, Senior Lecturer, Paediatric Department, Hospital Universiti Sains Malaysia (USM)

Statistician:

Dr. Najib Majdi bin Yaacob, Lecturer, Department of Biostatistics and Research Methodology, Hospital Universiti Sains Malaysia (USM)

Introduction:

Diabetes Mellitus is a chronic, complex metabolic disorder characterized by elevated levels of blood glucose resulting from defective of secretion, insulin resistance or both. Inadequate insulin secretion and diminished tissue response to insulin lead to abnormalities in carbohydrate, fat, and protein metabolism. (5) The etiology of diabetes mellitus is heterogeneous. Most cases are classified into two broad etiopathogenic categories: type 1 and type 2 diabetes mellitus. (1) Type 1 diabetes mellitus, characterized by a deficiency of insulin secretion, remains the most common form of diabetes in the young population. In contrast, type 2 results from a combination of resistance to insulin action and inadequate compensatory insulin secretory response from the degree of insulin resistance. (16)

Diabetes is the most common chronic endocrine disease, causing long-term complications affecting the eyes, kidneys, nerves, and blood vessels. Atherosclerotic lesions develop slowly but steadily from childhood, and though to accelerate when a child is diagnosed with diabetes mellitus, as described by many studies on children. (7,17). In this study, the researcher will focus on cardiovascular risks, specifically hypertension and dyslipidemia as complications of diabetes mellitus among the pediatric population. Cardiovascular disease is the chief cause of morbidity and mortality among diabetic patients. (17) Based on a study from India, poorly controlled diabetes causes about 5% of all global deaths each year due to cardiovascular complications. Furthermore, cardiovascular risks contribute to a high incidence of macrovascular complications among people with diabetes, leading to significant health burdens and increasing the health care cost in the community. (17)

Worldwide study of cardiovascular risk estimates the prevalence of hypertension in at 15-20%, and dyslipidemia at 60-80% in children with diabetes mellitus. Based on the EURODIAB IDDM complication study, the complications of diabetes related to an increase in the duration of diabetes, age, and poorly controlled diabetes based on HbA1c reading. (7) Schnell et al. found that identifying risk factors and immediate management reduced mortality and remarkably improved life expectancy due to cardiovascular disease and coronary heart disease. (7,16)

Hence, this study aims to identify the prevalence and associated risk factors for hypertension and dyslipidemia among patient with diabetes mellitus in the pediatric group.

Problem statement and study rationale

Diabetes mellitus is a significant health problem that can lead to macrovascular and microvascular complications. Cardiovascular complications such as dyslipidaemia and hypertension are substantial causes of morbidity and mortality among diabetic patients. In patient with poorly controlled diabetes mellitus, cardiovascular diseases such as hypertension and dyslipidemia appear at a younger age than in the general population. The SEARCH for Diabetes in Youth Study (SEARCH) in 2014 discovered that significant complication has severe effects on individual's quality early in life.

Minimal studies have been conducted among diabetics in the pediatric population compared to adults, particularly in Malaysia. As a result, there is not enough data for the researchers to identify the risk factors for hypertension and dyslipidaemia. Therefore,

conducting this study may help in identifying risk factors and, at the same time, allow us to take early action to reduce risks and improve health outcomes in the future.

Research Question:

1. What is the prevalence of Hypertension and Dyslipidaemia in Diabetes Mellitus among the Paediatric Population?

2. What are the risk factors for Hypertension and Dyslipidaemia in Diabetes Mellitus among Paediatric Population?

The objective of the study:

General:

To determine the Prevalence and Risk Factors for Hypertension and Dyslipidaemia in Diabetes Mellitus among Paediatric Population, Hospital Universiti Sains Malaysia (USM), Kelantan

Specific

To estimate the Prevalence of Hypertension and Dyslipidaemia in Diabetes Mellitus among Paediatric Population, Hospital Universiti Sains Malaysia (USM), Kelantan.

To identify the Risk Factors for Hypertension and Dyslipidaemia in Diabetes Mellitus among Paediatric Population, Hospital Universiti Sains Malaysia (USM), Kelantan.

Research Hypothesis:

Social demographic, anthropometric measures, clinical diabetes, and biochemical profiles are important risk factors for hypertension and dyslipidaemia in diabetes mellitus among the pediatric population.

Literature review

Diabetes mellitus, according to the World Health Organization (WHO), is a metabolic disorder of multiple etiologies that is defined by chronic hyperglycaemia. It is related to disturbances in carbohydrate, fat, and protein metabolism due to defects in insulin secretion, insulin action, or both. The effects of diabetes include long-term damage and dysfunction that lead to the failure of various organs. The long-term complications of diabetes mellitus include the progressive development of specific complications such as peripheral vascular and cerebrovascular disease.

This study will focus on the risk factors for hypertension and dyslipidaemia in diabetes mellitus among the pediatric population in Malaysia. There is no publication regarding this study in Malaysia. The only data available comes from the Malaysian Ministry of Health's (MOH) Diabetes in Children and Adolescents Registry (Di CARE). The data, however, are limited due to the small population and not including the whole of Malaysia. According to Di CARE data from 2012, the prevalence of hypertension and dyslipidaemia ranged from 4% to 5% in DM1 to 16-20% in DM2.

Childhood-Onset Type 1 Diabetes and Cardiovascular Disease by Perchard R, Amin R. Diabetes Management 2015;5(3):215–27

Diabetes is the most common childhood endocrine disease, and it is associated with an increase in cardiovascular and peripheral vascular risks. Chronic hyperglycaemia accelerates different phases of atherogenesis, causing artery walls to harden and thicken, resulting in early manifestations of vascular dysfunction in a diabetic individual. There are some modalities used to estimate the cardiovascular risks of diabetes. A study by Manuel A. et al. (2011) mentioned that carotid intima-media thickness (IMT) is related to cardiovascular risk factors and disease. The ultrasound measurement makes it possible to detect thickening in the initial phases of atherosclerosis. Diabetes mellitus patients have a higher prevalence of intima-media thickness and carotid injury.

Factors Affecting Cardiovascular Risk in Children, Adolescents, and Young Adults with Type 1 Diabetes by Stankute I, Dobrovolskiene R, Dante E, Razanskaite-Virbickiene D, Jasinskiene E, Mockeviciene G, et al. 2019;2019

In a recent study of 883 diabetic participants aged 1 to 25 years old, Ingrida Stankute et al. (2019) discovered that hypertension is present in 29.8% of cases and dyslipidaemia is present in 62.6%. According to the study, hypertension is higher in males (34.5%) than in females (26.1%); p-value = 0.007. Diabetes-related hypertension was more common in people who were overweight (40.6%) or obese (65.6%) than in people who were of average weight (25.6%) (p-value<0.05). Dyslipidaemia, on the other hand, was more common in the poor glycaemic control group than in the optimum glycaemic control group (69.9% vs. 53.6%, respectively) (p<0.001). This study also discovered that HbA1c was higher in individuals with dyslipidaemia compared to patients with normal lipid levels.

Prevalence, Awareness, and Treatment of Hypertension in Patients with Diabetes Type 1: A Nationwide Multicentre Study in Brazil Int J Hypertens by Gomes MB, Tannus LRM, Matheus ASDM, Cobas RA, Palma CCS, Silva ATK, et al. 2013;2013

This nationwide multicentre study, conducted in 28 public clinics in 20 Brazilian cities, indicated that the prevalence of hypertension in T1DM patients is 19.6% among 689 individuals, with children and adolescents having a prevalence of 8.3%. This study which conducted by Marilia B. Gomes et al., published in 2013, revealed that the prevalence of hypertension has increased fourfold in overweight and obese children and adolescents in the diabetes mellitus population. This hypertension prevalence is comparable to that reported in a SEARCH study in 2010 (5.9%).

Dyslipidaemia in Young Patients with Diabetes Mellitus Type 1. Arch Endocrinol Metab by Homma TK, Endo CM, Saruhashi T, Mori API, de Noronha RM, Monte O, et al. 2015;59(3):215–9

Thais Kataoka Homma et al. discovered 72.5% dyslipidaemia among 239 participants with T1DM in a research conducted at Santa Casa School of Medicine in Sao Paulo, Brazil, from 1998 to 2012. The number of participants was greater in females (81.7%) than in males (61.8%), with $p<0.01$. The higher rates of dyslipidaemia are associated with puberty, being overweight, and gender. Another research published in 2006 by Franca and Alves discovered that dyslipidaemia affects 81.7% of diabetic patients. Both studies in Brazil found that being overweight and obese is a major risk factor for dyslipidaemia in children and adolescents with diabetes. The studies concluded that early identification of high-risk groups might help to prevent or delay the onset of cardiovascular risk.

The SEARCH for Diabetes in Youth Study: Rationale, Findings, and Future Directions. Diabetes Care by Hamman RF, Bell RA, Dabelea D, D'Agostino RB, Dolan L, Imperatore G, et al. 2014;37(12):3336–44.

This SEARCH study, published by Hamman RF et al., discovered a high prevalence of elevated blood pressure, 23.7% among youth with T2DM. This is about four times the rate of 5.9% for T1DM among the youth. The SEARCH study is an ongoing multicentre study that undertakes population-based ascertainment of cases of non-gestational diabetes mellitus in youth aged below 20. The study found that minority ethnicity, higher BMI, and HbA1c were independently associated with a higher prevalence of elevated blood pressure in youth with T1DM. A similar pattern was found among the youth with T2DM; however, they did not always attain statistical significance, most likely due to insufficient power given their small size.

Dyslipidaemia in Type 1 Diabetes Mellitus: Relation to Diabetes Duration, Glycaemic Control, Body Habitus, Dietary Intake and Other Epidemiological Risk Factors by Mona HM, Sahar SA, Hend SM, Nannies A-WA 2015;63(2):63–8

Hassan M. Mona et al. published a research in 2015 that demonstrated dyslipidaemia in a considerably larger percentage of children and adolescents with T1DM, (65%) compared to 28.2% non-diabetic among 60 children aged 9-16 years old at Cairo University Children's Hospital. These findings were comparable to those of Rahma et al. (2006), who discovered that 66% of the children with dyslipidaemia were more likely to be female compared to 34% of the non-diabetic children (p=0.025). However, study results reported by Alrabaty et al. (2009) and Patiakas et al. (2007) found

no association between lipid abnormalities in children and adolescents with T1DM and gender. Furthermore, Teles and Fornes (2012) and Guy et al. (2009) discover a link between poor glycaemic control and increased dyslipidaemia. Physical inactivity, according to Shaw et al. (2006) and Muchacka-Bianca et al. (2006), is a possible risk factor for dyslipidaemia in type 1 diabetes mellitus.

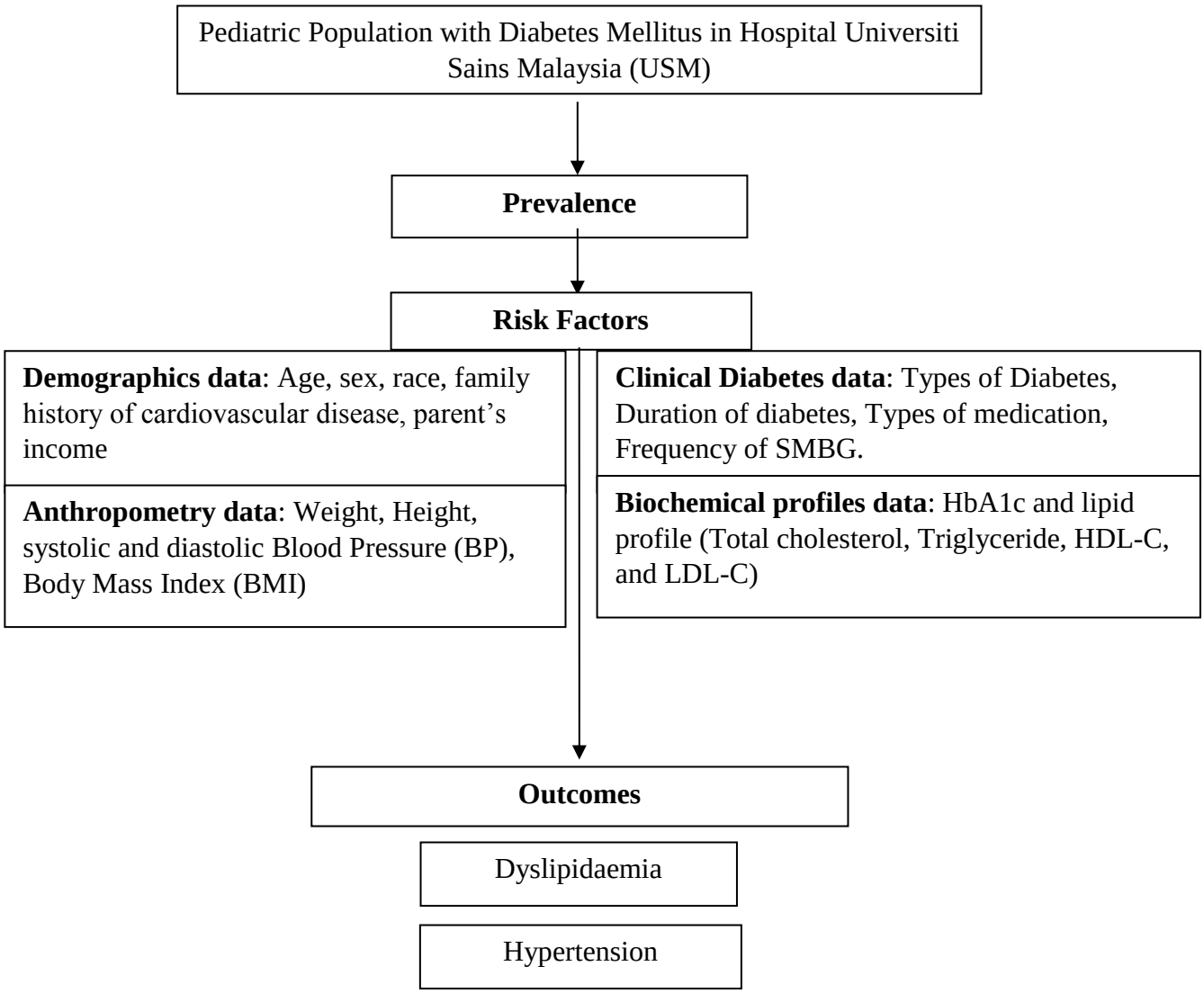
The Prevalence of Dyslipidaemia and Associated Factors in Children and Adolescents with Type 1 Diabetes by Bulut T, Demirel F, Metin A. J Pediatr Endocrinol Metab. 2017;30(2):181–7

Dyslipidaemia was found in 26.2% of 202 children and adolescents with T1DM aged 3-18 in a study published by Bulut T et al. (2016). This study's most common findings were hypercholesterolemia (15.8%) and hypertriglyceridemia (12.9%). Age, body mass index (BMI), HbA1c value, and poor metabolic control were significantly higher in cases of dyslipidaemia. Dyslipidaemia is common in children and adolescents with type 1 diabetes mellitus, according to the study's findings, and it worsens with age. Therefore, lipid levels in patients with type 1 diabetes should be closely monitored and education on healthy eating should be emphasized.

There are no specific studies on the cardiovascular risk of diabetes mellitus in the Malaysian pediatric population. One survey by Alyaa Al-Khateeb et al. found cardiovascular disease in approximately 19.6% of adults with diabetes. The study discovered that people with cardiovascular disease had diabetes for significantly longer than those without cardiovascular disease, with a p-value=0.03. Total cholesterol was considerably higher in patients with cardiovascular illness (p=0.02), whereas HDL was significantly lower (p=0.01). The major independent risk factors for cardiovascular

disease are a family history of premature cardiovascular disease (OR = 1.5, CI 95% : 1.1-3.6), duration of diabetes (OR = 2.1, Cl 95% : 0.9-2.6), total cholesterol level (OR = 1.4, Cl : 1.0-1.7) and HDL-C level (OR = 0.5, Cl 95% : 0.2-1.0). This study demonstrates that detecting and treating dyslipidaemia early can help reduce the prevalence of atherothrombosis and cardiovascular disease in diabetic patients.

Conceptual Framework:



Research design:

Retrospective cohort study, revision of 15 years of cases from 2004-2019.

Study Area:

Paediatric Endocrine Clinic, Paediatric Department and Medical Record Department, Hospital Universiti Sains Malaysia (USM), Kubang Kerian, Kelantan.

Study Duration:

June 2020 – June 2021 (1 year)

Study Population:

All pediatric population diagnosed with diabetes mellitus attended the Paediatric Endocrine Clinic at Hospital Universiti Sains Malaysia (USM), Kubang Kerian, Kelantan.

Subject Criteria

Inclusion criteria:

1. Pediatric Population with Diabetes Mellitus
    a) Diagnosed or/and on treatment under Paediatric Endocrine Clinic, Hospital USM, Kelantan.
    b) Diagnosed at least six months from the onset.
2. Pediatric age group
    a) Age below 18 years old on the diagnosis of diabetes mellitus

Exclusion criteria:

1. Hypertension and dyslipidemia are secondary to other causes or underlying chronic illnesses.

Sample Size Estimation:

Objective 1.

The sample size calculates using the formula for estimating a population's proportion as below.

$$n = \left(\frac{Z}{\Delta}\right)^2 P(1-P)$$

Where n is the calculated sample size, Z is the critical value corresponding to the confidence level, Δ is the one-sided precision of estimation (margin of error), and P is the proportion of patients with the outcome of interest obtained. To estimate the population's prevalence to a 95% level of confidence, the calculated sample size is summarized in the table below.

Variable	Proportion	Reference	Precision of estimate	Calculated sample size
Hypertension	29.8%	Hindawi 2019, Journal of Diabetes Research Factor affecting Cardiovascular Risk in children, Adolescents, and youth with Type 1 Diabetes	10%	81
Dyslipidaemia	62.6%		10%	90

Objective 2.

The sample size was calculated using the formula for the comparison of two independent means (for independent numerical variables) and the comparison of two independent proportions (for categorical independent variables) for each outcome (hypertension and dyslipidemia) using PS software.

We are interested in examining whether age, gender, race, socioeconomic status, anthropometry data, glycaemic control, duration of diabetes, and frequency of SMBG monitoring were important risk factors for hypertension and dyslipidaemia.

The calculated sample size was summarized in the tables below with a type I error of 5% and Type II error of 20%.

Sample size calculation for two independent means.

Variable	Standard deviation among patients without outcome	Reference	Estimated difference	The ratio between groups (M)	Calculated sample size
Outcome: Hypertension					
Age	5.6	Hindawi, Journal of Diabetes Research 2019, Factor affecting cardiovascular risk in children, adolescents, and young adults with type 1 diabetes	3	2	126
Duration of Diabetes	4.8		3	2	93
Frequency of SMBG	No previous study regarding this variable				
Outcome: Dyslipidaemia					
Age	3.9	Journal of pediatric endocrine and metabolism 2016, The prevalence of dyslipidemia and associated factor in children and adolescent type 1 diabetes.	3	0.5	60
Duration of Diabetes	3.05		3	0.5	38
Frequency of SMBG	No previous study regarding this variable				

Sample size calculation for two independent proportions.

Variable	The proportion among those without outcome (P0)	Reference	The estimated proportion among those with the outcome (P1)	The ratio between groups (M)	Calculated sample size
Outcome: Hypertension					
Gender (female)	32.3	Journal of Paediatric, Prevalence and correlates of elevated blood pressure in Youth with Diabetes mellitus: The search for Diabetes in Youth	57.3	2.0	132
Race (Malay)	34.7		59.7	2.0	135
Socio-economic status	No previous study regarding this variable				
Compliance					
BMI (obesity)	29.5	International Journal of Hypertension, Prevalence, awareness, and treatment of hypertension in a patient with type 1 diabetes: A nationwide multicentre study in Brazil 2013	54.5	2.0	129
Outcome: Dyslipidaemia					
Gender (Female)	41.4	Journal Paediatric endocrine and metabolism 2016, the prevalence of dyslipidemia and associated factor in	61.4	0.5	132