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Review Article

Why Does the Poor Glycemic Control Among Type 2 Diabetes Mellitus Patients Remain High in Southeast Asia?

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ABSTRACT

Presently, as well, 55% of the world's diabetic population is Asian, with an estimated 230 million. The International Diabetes Federation (IDF) shows that the number of people with diabetes in the Southeast Asia (SEA) Region is 16.8% of all people with diabetes worldwide. To manage a patient's blood glucose level, consider minimizing the worst effects of diabetes mellitus. Glycemic control using HbA1c levels is one of the important factors in the risk of diabetes that is associated with complications and mortality. A PubMed and Google Scholar databases were searched using the following: We only screened original-type articles for relevance and considered them further. Type 2 diabetes mellitus patients in Southeast Asia mostly experience uncontrolled blood glucose. More than 50% of research subjects show poor glycemic control. The influencing factors of poor glycemic control in Southeast Asia were age, BMI, hypertension, smoking activity, education, physical activity, and dyslipidemia. The awareness of glycemic control must be improved in type 2 diabetes mellitus patients.

INTRODUCTION

Presently, about 230 million Asians have hyperglycemia, which accounts for generally 55% of the world's diabetic people. Two Asian countries, China (around 110 million) and India (around 69.2 million), have the largest number of patients with diabetes in the world. Three other Asian countries, Indonesia, Japan, and Bangladesh, are also ranked among the countries with the largest number of patients with hyperglycemia worldwide (Yang et al., 2019). The International Diabetes Federation (IDF) Diabetes Atlas shows that the number of individuals with diabetes in the Southeast Asia SEA Region is 16.8% of people with diabetes worldwide (Atlas Diabetes, 2021).

Complications such as cardiovascular disease, neuropathy, nephropathy, and retinopathy are major problems of long-term diabetes. The life-threatening issue could happen as a consequence of impairment in various organs and can lead to those complications (Afroz et al., 2019). Uncontrolled diabetes is linked with mortality from cardiovascular disease. Glycemic control is a very crucial target in the treatment of people with type 2 diabetes mellitus. It persists as the most important therapeutic goal for the anticipation of organ impairment, and more complications occur from diabetes (Yosef et al., 2021).

It is crucial to keep a patient's blood glucose level within the standard or close to the standard range to reduce the burden of diabetes mellitus (Yosef et al., 2021). Glycemic control, measured by hemoglobin A1c (HbA1c), is a contributing factor for diabetes mellitus-related complications and loss of life. Patterns with regularly high HbA1c in the long term are linked with an elevated risk of complications and high mortality rates (Luo et al., 2017).

The privilege of using HbA1c rather than plasma glucose is generally known, as is the potentiality of HbA1c to give a diagnosis of glucose levels over several months. Recently, the American Diabetes Association's (ADA)

recommendation that hemoglobin A1c (HbA1c) levels be 6.5% (47.5 mmol/mol) has been included as one of the diagnostic standards for diabetes. The consequences of being diagnosed this way are that you do not have to abstain from food. Diabetes is diagnosed at an HbA1C of greater than or equal to 6.5% (American Diabetes Association, 2021).

This review aimed to assess the prevalence and factors contributing to poor glycemic control in type 2 diabetes mellitus patients in Southeast Asia.

METHODS

Data sources and searching strategy

Following the PRISMA guideline, PubMed, Medline, and Google Scholar were utilized for relatable articles. Databases were searched using the following keywords: HbA1c, fasting blood glucose, fasting plasma glucose, poor glycemic control, type 2 diabetes mellitus, and Southeast Asia, Indonesia, Singapore, Malaysia, Brunei Darussalam, Thailand, Vietnam, the Philippines, Myanmar, Cambodia, and Laos. We only screened original-type articles for relevance and considered them further. The last surveillance was performed on December 31, 2022.

Data extraction, quality assessment, and report

Inclusion criteria of articles that were observational research, including cohort, cross-sectional, case control, and case-report research Additionally, we included the studies that provide information related to this topic in full text. Only articles published between 2017 and 2022 are included in this review. The editorial letter or viewpoint and non-English articles were excluded. Studies considered focused on poor glycemic control and its causes.

The selected articles were screened again to identify relevant articles related to our topics. We eliminated duplicated articles. Two investigators independently reviewed articles, including titles, abstracts, and full-text articles, using inclusion and exclusion criteria. We appraised the articles using the Joanna Briggs Institute (JBI) Critical Appraisal Tools (Briggs, 2017). Disagreements were resolved through discussion. The studies were screened for reporting the prevalence of poor glycemic control and factors contributing to it in the SEA region. We conducted the PRISMA checklist and flowchart diagram to report on the articles reviewed.

RESULTS

Identification of abstracts

From the 188 articles found in the search through PubMed, we screened the abstracts that related to the topic from each country: Indonesia = 7, Singapore = 16, Malaysia = 16, Brunei Darussalam = 0, Thailand = 14, Vietnam = 6, Philippines =4, Myanmar = 0, Cambodia = 0, and Laos = 0. Total = 64. For Myanmar and Cambodia, we searched thoroughly on Google Scholar for articles related to the topic because these two countries have zero entries in PubMed. Exclusion of studies that are not related to each country, meta-analysis, and systematic review articles Seven final articles were chosen from a pool of 64 publications.

Table 1. Articles found in searches

Keyword (using Country)	Number of original articles (since 2017-2022)
Indonesia	20
Singapore	39
Malaysia	52
Brunei Darussalam	-
Thailand	46
Vietnam	12
Philippines	15
Myanmar	1
Cambodia	2
Laos	1
TOTAL	188

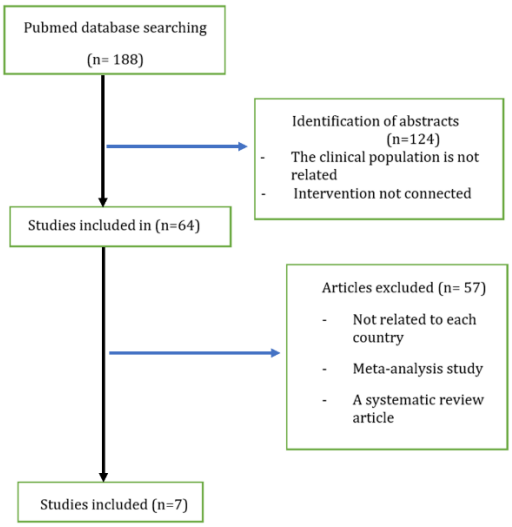


Figure 1. Flowchart Diagram showing literature search

Table 2. The prevalence of poor glycemic control in Southeast Asia

Author, year	Country	Methods	Result
(Eugenia et al., 2022)	Indonesia	This research used an observational analytic study with a cross-sectional design at Dr. Soetomo General Academic Hospital from October 2020 to March 2021. T2DM patients matched the inclusion criteria at 43.	39 people (90.70%) are patients with uncontrolled blood glucose. And four people had controlled blood glucose (9.3%).
(Bancks et al., 2015)	Singapore	This research used a cohort prospective design with a total of 5,770 men and women in the Singapore Chinese Health Study, who delivered a blood sample.	Over 50% of the research population had HbA1c $\leq$ 5.7%.
(Ismail et al., 2016)	Malaysia	T2DM patients matched the inclusion criteria with 127 medical records in the UKM Medical Centre. This study used a cross-sectional design.	About 21.3% of patients who achieved good glycemic control.
(Haskani et al., 2022)	Brunei Darussalam	135 subjects were interviewed for this study, which was located in Kuala Belait. This study used a cross-sectional design.	About 86,49% of subjects have poor glycemic control.
(Puangpet et al., 2022)	Thailand	The total number of participants is about 488. T2DM subjects aged > 35 years from 25 central health care in Samutsakhon, Thailand, were managed from February 2018 to March 2019. And this study following method with a cross-sectional study design.	41% of females and44% of males have good glycemic control, as defined by HbA1C < 7%.
(Thuy et al., 2021)	Vietnam	There are 189 patients who agreed to be participants in this study. This study was managed in October 2019 among diabetes patients at a hospital in Hanoi, Vietnam. This research design is an observational, retrospective, longitudinal cohort survey.	Only 36.1% patients having HbA1c < 7.0%.
(Vonglokham, et al., 2019)	Laos	The total sample used in this study is 2492 individuals aged 18–64 years. This study used a cross-sectional design.	Only 26.4% of those treated had good glycemic control.

Note: The table above shows that patients with type 2 diabetes mellitus in Southeast Asia mostly experience uncontrolled blood glucose. More than 50% of research subjects show poor glycemic control in patients with type 2 diabetes mellitus, such as in Indonesia at 90%, Malaysia at 78%, and Laos at 73.6%.

Table 3. Factors contributed in each country

Country	Factors
Indonesia	Gender, education levels, age, diabetes duration, hypertension, dyslipidemia, obesity, and smoking activity
Singapore	Age, female, race, education, smoking status, alcoholic drinks/week, physicalactivity, BMI, hypertensive
Malaysia	Age, gender, ethnicity, educational level, marital status, and occupation
Brunei Darussalam	Age, gender, race, education level, occupation, family history, duration since diagnosis with T2DM, participants' antidiabetic therapy
Thailand	Age, duration of disease (years), BMI, underlying diseases (hypertension, dyslipidemia, ischemic heart, stroke, gout), lifestyle, family history of CVD
Vietnam	Gender, living location, education, age, hypertension, dyslipidemia, diabetic medication, period of diabetes, number of comorbidities, polypharmacy, DMI, start HbA1C level, last HbA1C, behavioral characteristic
Laos	Age, sex, education, employment status, marital status, residence, BMI, central obesity, nutritional food, physical activity, current tobacco use, and alcohol drinking

Table 4. Factors contributed to uncontrolled blood glucose

No	Factor	Description
1.	Gender	There is no significant difference between genders in controlled glucose levels in all countries in Asean.
2.	Age	There are statistically significant differences between the two countries in Asean, namely Singapore and Laos. Within the sample quantity of Singapore, there are 5770 samples, and in Laos, there are 2492 samples.
3.	Education	There are statistically significant differences in the 3 countries in Asean, namely Singapore, Malaysia, and Brunai Darussalam. Within Singapore has 5770 samples, Malaysia 127 samples, and Brunai 135 samples.
4.	Diabetic duration	There are statistically significant differences in one country in Asean, namely Thailand, with 488 samples.
5.	Familyhistory	There is no significant difference between family history and controlled glucoselevels in all countries in Asean.
6.	Hypertension	There are statistically significant differences between the two countries in Asean, namely Singapore and Laos. The sample quantity in Singapore is 5770, and in Laos there are 2492 samples.
7.	Dyslipidemia	There are statistically significant differences in one country in Asean, namely Laos, with 2492 samples.
8.	Smoking activity	There are statistically significant differences between the two countries in Asean, namely Singapore with 5770 samples and Thailand with 488 samples.
9.	BMI	There are statistically significant differences between the two countries in Asean, namely Singapore and Laos, which is that each country has 5770 samples for Singapore and 2492 samples for Laos.
10.	Physical activity	There are statistically significant differences in one country in Asean, namely Laos, with 2492 samples.

DISCUSSION

The ADA guidelines advise treatment to advance with an extra drug if monotherapy does not reach the HbA1c goal's level after three months. The sort of third-line treatment involves insulin initiation or a triple variety of oral diabetic drugs. (Ji et al., 2021). The American Association of Clinical Endocrinology (AACE) treatment guidelines suggest that patients with an HbA1c level of 7.5% or higher (≥59 mmol/mol) should initiate a sequence of metformin and diabetic drugs (Garber et al., 2020). Even though intensive glycemic control has been the principal target for the therapy of diabetic patients for several years, research indicates that reaching an HbA1c < 7% is not associated with cardiac and vascular advantage.

The primary target of medication for diabetes mellitus is a near-normal blood glucose level.

Poor glycemic control is one of the major risks for macro- and microvascular complications. And all these complications can lead to higher morbidity and mortality related to diabetes mellitus (Roy and Jha, 2022). Accordingly, moving the goal of DM prescription to lower the risk of enlarge hyperglycemia complications compared with lower glucose levels And HbA1c levels need to be explained with awareness in patients who habitually experience comorbidities. The situation is related to mistakenly enlarged HbA1c levels such as anemia (iron, B12, and folic acid deficiency), chronic kidney disease, or functional asplenia (Kaiafa et al., 2021).

The results of the research show poor glycemic control in patients with type 2 diabetes mellitus in Southeast Asia: Indonesia, 90%, Singapore, over 50%, Malaysia, 78%, Brunei Darussalam, 75%, Thailand, 59%, Vietnam, 64%, and Laos, 74%. The factors found to influence good glycemic control in the study review were age, BMI, hypertension, smoking activity, education, physical activity, dyslipidemia, and diabetic duration.

Age

Diabetes mellitus is correlated with increased biological age. The increase in age is along an ordered line in settings with glucose consumption disregarding the pathophysiological system. So there is a strong connection between HbA1c and the age proportion, the major factor in glucose control (Bahour et al., 2022). Some studies described glycemic control as better among the older age groups than the young and middle age groups. There is evidence that information about diabetes is more common among older people (Shamshirgaran et al., 2017). This research also shows that older people are more aware of their diabetes condition. The older group was taking medication more often than the younger ones (Vonglokham et al., 2019).

A younger age at diagnosis of diabetes is associated with a seriously lower risk of incident comorbid outcomes. Patients who diagnose diabetes at 50–59 years of age or younger are crucially more at risk of heart disease than patients who diagnose diabetes melitus at 70 years of age or older (Cigolle et al., 2022).

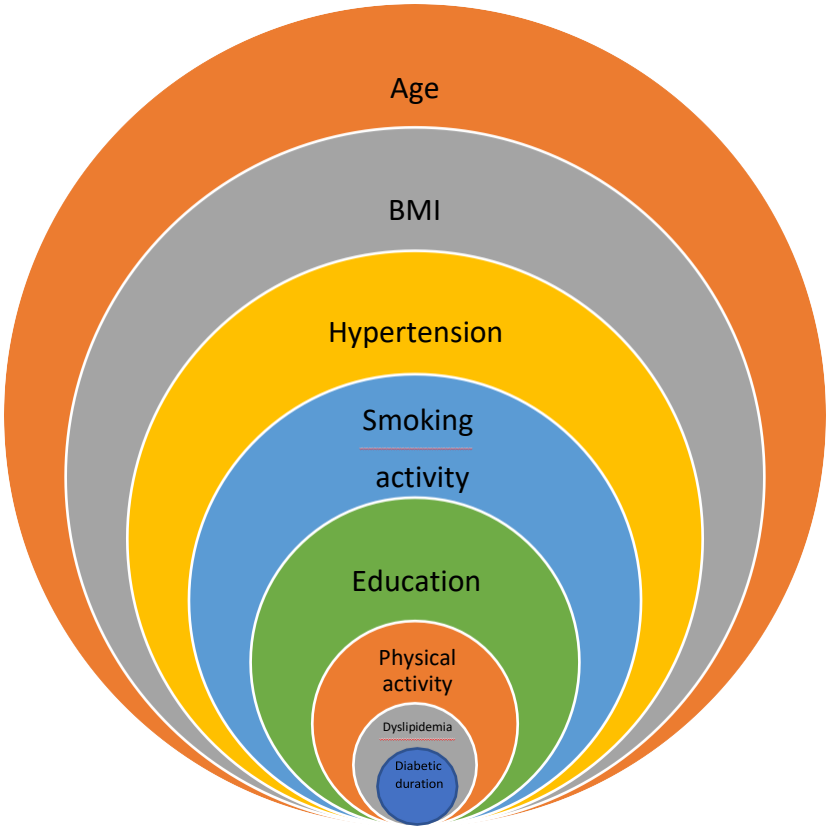


Figure 2. The diagram shows factors contributing to uncontrolled blood glucose.

BMI

Overweight is the major risk factor for diabetes mellitus type 2 development (Chen et al., 2018). Type 2 diabetes and obesity are associated with resistance to insulin. Most individuals with a high BMI are insulin resistant, which means pancreatic β-cells make adequate numbers of insulin that are resistant to overcoming insulin level cutting under normal circumstances to maintain normal glucose (Al-Goblan et al., 2014). In fact, increased body fat mass is connected with decreased fasting blood glucose and insulin levels, higher oral glucose tolerance and insulin sensitivity, and an increased possibility of type 2 diabetes mellitus (Klein et al., 2022).

Besides that, the doctors will prescribe antidiabetic medicine to normal-weight patients. This can make the medicine ineffective at controlling blood glucose levels if the patient is overweight or obese (Deng et al., 2019). Treatments that decrease obesity's rate in people with diabetes mellitus type 2 could improve health outcomes (Boye et al., 2021).

Hypertension

Chronic hyperglycemia plays a major role in the induction of vascular problems in diabetes and demands some mechanisms as well as increased forming of advanced glycation end products (AGEs) and triggering oxidative stress and swelling cells. Hypertension is a major risk component for diabetes-associated vascular complications because hypertension is identified by vascular dysfunction (Petrie et al., 2018). Diabetes mellitus may once contribute to high blood pressure by enlarge renal sodium holding. This situation may cause a further increase in insulin resistance, producing a chain reaction that may lead to the enlargement of hypertension and diabetes. In addition, aversion of insulin is also related to a lower vasodilation response to insulin in substance and an enlarged vasoconstrictor acknowledgment to several vasopressors, which, on the whole, results in a higher systolic blood pressure (Yan et al., 2016).

Smoking activity

The body's cells could be dysfunctional because of the chemicals in cigarettes. Cigarettes's substance can cause swelling throughout the body, which may reduce the potency of insulin. Furthermore, when elements from tobacco smoke collide with oxygen in the body, this action can also cause cell destruction. Both oxidative stress and cell damage and swelling are conceivably related to the threat of hyperglycemia (Sliwinska-Mosson and Milnerowicz, 2017). High concentrations of nicotine can reduce the effectiveness of insulin. Smoking makes controlling hyperglycemia and regulating insulin levels more burdensome because smokers depend on more insulin to control blood glucose levels ("Cigarette Smoking: A Risk Factor for Type 2 Diabetes | FDA," n.d.).

Education

Greater educational attainment compared with no formal schooling was associated with a significant diabetes risk (Seiglie et al., 2020). The great educational level was remarkably linked with a better consciousness of diabetes complications. The percentage of patients with high glycemic levels was high in this study. An academic degree may not be a good prognostic for better therapeutic obedience. Regardless of the worthy importance of appropriate diet and physical activity in the control of diabetes, there was an overestimation of poor food and low physical activity. Possibly for good glycemic control, education was one of the highlights of the attachment to treatment prescriptions as a whole, especially to a dietary program and workout program for consistent effort (Al-Rasheedi, 2014).

Physical activity

Concerning the meaning of physical activity, it is a complete movement set up by skeletal muscle that develops energy beyond the resting level. Physical activity or exercise is frequent and constant massive muscle movement, such as walking, swimming, cycling, and jogging (Wake, 2020).

Physical activity or exercise can increase insulin activity in liver and muscle. Advance activity of insulin be allowed for 24 hours after about 20 minutes maximal exercise (Colberg et al., 2016). Intense physical exercise can decrease inflammation of pancreas and oxidative stress tissue. Action of insulin has the most purpose in muscle tissue (Yang et al., 2019). Having 3 times a week for minimum 60 minutes each period during 2 months could lower blood glucose and HbA1c level (Kurniawati et al., 2020).

Dyslipidemia

Patients with type 2 diabetes mellitus often have higher serum triglyceride levels. It should be acknowledged that these lipid changes are essential to the adjustment in lipid profile seen in obesity and the insulin resistance syndrome.

People with type 2 diabetes mellitus have high numbers of triglycerides, a small, dense LDL, and a decreased HDL-C level (Subramanian and Chait, 2020).

Arteriosclerotic vascular disease is the result of hyperlipidemia. Diabetes mellitus type 2 is associated with low levels of HDL, whose major role is to benefit the cholesterol discharge from cells and keep an essential balance of component lipids in the cell membranes (Kane et al., 2021).

Lipid abnormal level is usual in person with type 2 diabetes mellitus. Higher level triglycerides mostly similar with poor glycemic control in general hyperglycemia patients. Points that associated to good HbA1c levels were lower levels of total cholesterol, LDL-C, and triglycerides (Haghighatpanah et al., 2018).

An abnormal lipid level is usual in people with type 2 diabetes mellitus. Higher levels of triglycerides are mostly similar to poor glycemic control in general hyperglycemia patients. Points that were associated with good HbA1c levels were lower levels of total cholesterol, LDL-C, and triglycerides (Haghighatpanah et al., 2018).

Diabetic duration

For individuals with short-term diabetes, good HbA1C levels are related to a reduced risk of death. Good glycemic control may be advantageous in people with short periods of diabetes, whereas a less stringent target may be guaranteed with longer diabetes exposure. The duration of type 2 diabetes mellitus was clearly correlated with glycemic control (Ghouse et al., 2020).

A longer period of diabetes resentfully concerns glycemic control; it may be due to a lower insulin secretion or inadequate insulin in patients. Patients with diabetes for one decade or more were convincing to have high glycemic level variability as opposed to patients who had hyperglycemia for less than 3 years. A longer period of having a diabetic problem is one of the components that leads to poor glycemic control (Haghighatpanah et al., 2018).

CONCLUSION

This study tries to answer the following research question: what is the association between poor glycemic control-related complications in patients with type 2 diabetes mellitus in Southeast Asia? More than 50% of research subjects show poor glycemic control in patients with type 2 diabetes mellitus in Southeast Asia (Indonesia 90%, Singapore over 50%, Malaysia 78%, Brunei Darussalam 75%, Thailand 59%, Vietnam 64%, and Laos 74%). Factors that contribute to poor glycemic control are age, BMI, hypertension, smoking activity, education levels, physical activity, dyslipidemia, and diabetic duration.

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