

HbA1c Variability and its Associated Factors among Type 2 Diabetes Patients in Malaysian Public Primary Care Clinics

Xin Rou Teh¹, Aslene Siu Tjing Yeoh², Azah Abd Samad², Mastura Ismail³, Feisul Mustapha⁴, Sheamini Sivasampu⁴

¹Institute for Clinical Research, National Institutes of Health, Shah Alam, Selangor, Malaysia

²Klinik Kesihatan Seksyen 7, Ministry of Health Malaysia, Shah Alam, Selangor, Malaysia

³Family Health Development Division, Ministry of Health Malaysia, Putrajaya, Malaysia

⁴Perak State Health Department, Ipoh, Perak, Malaysia

Corresponding author's email: xinrou1801@gmail.com

Introduction

- One in five adults in Malaysia are living with diabetes mellitus (DM) in 2019 (1).
- Literature demonstrated that visit-to-visit HbA1c variability is associated with diabetic complications (2,3).
- However, there was a paucity of literature on the factors associated with HbA1c variability.
- Age (4,5), gender (5,6), use of insulin (4), obesity or increased body mass index (BMI) (5,6), reduced high-density lipoprotein-cholesterol (HDL-C) (5) and ischemic heart disease (4) were shown to be associated with high HbA1c variability.

Objective

- To identify the factors associated with HbA1c variability in type 2 DM patients treated in Malaysian public primary care clinics.

Materials and Methods

Study design Retrospective cohort formed using electronic medical records from two public primary care clinics in Selangor

Study population We included all patients that fulfilled the following criteria:

- Type 2 DM patients age ≥ 18 years
- ≥ 2 years of follow-up
- ≥ 2 HbA1c readings

HbA1c variability measures

$$CV = \frac{SD}{Mean} * 100 \quad SD = \sqrt{\frac{\sum(x-mean)^2}{N}}$$

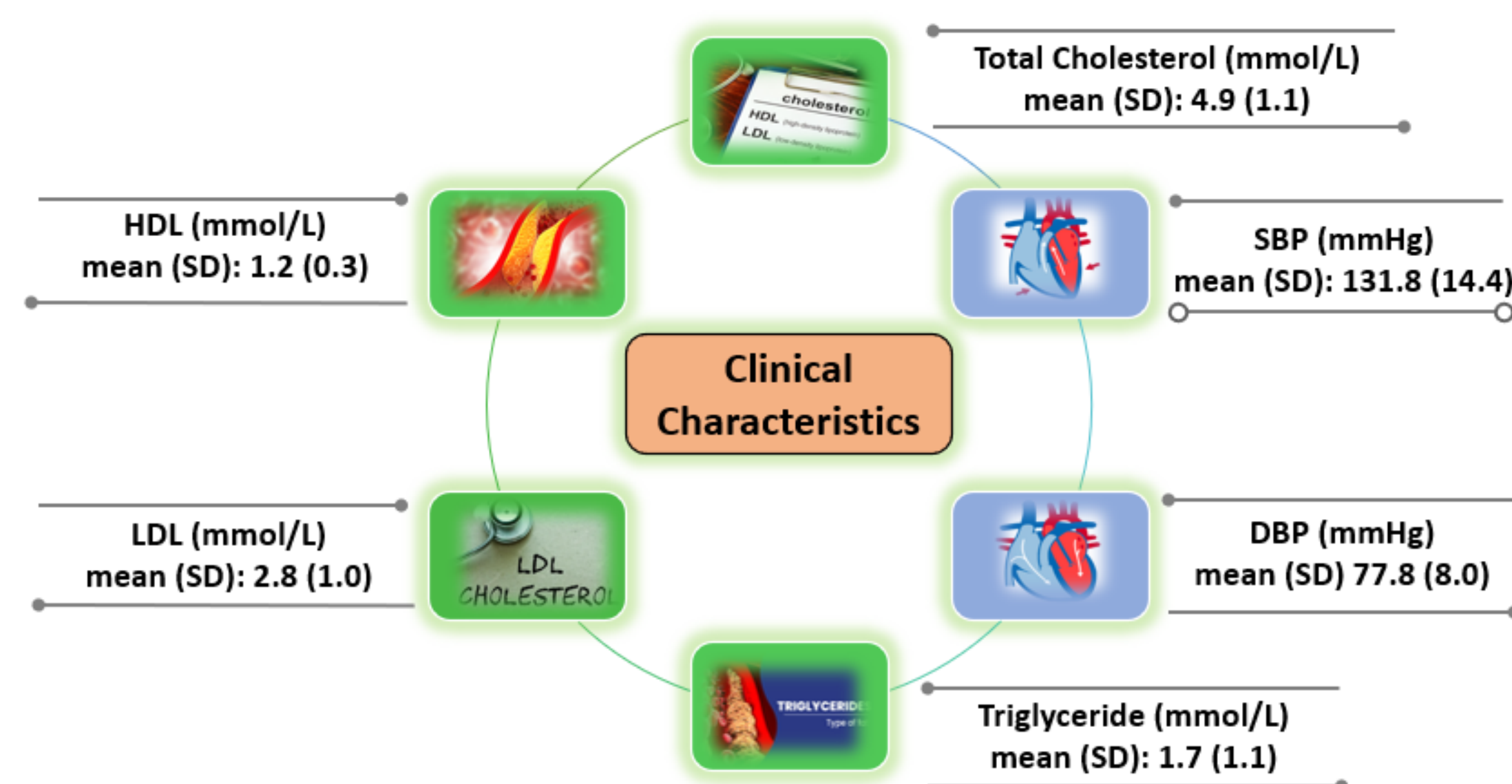
HbA1c-CV and HbA1c-SD will be categorized into high and low variability using their medians as the cut-off points.

Statistical analysis

- Logistic regressions were performed to explore the significant factors.
- The associations between the factors and HbA1c variability were reported using odds ratios (OR) and 95% confidence interval (CI)

Results and Discussion

- We included 2532 type 2 DM patients, with mean age of 61.7 years, more females (55.8%) and of Chinese ethnicity (39%).
- The mean duration of type 2 DM was 5.9 years, a mean BMI was 28.2 kg/m² and 45.8% of them were obese.
- Majority of the patients had hypertension as comorbid (73.5%), followed by chronic kidney disease (9.4%) and cardiovascular disease (2%).
- Only 30.7% of them had their HbA1c under control (HbA1c <7%).



SBP = Systolic blood pressure; DBP = Diastolic blood pressure; LDL = Low-density lipoprotein cholesterol; HDL = High-density lipoprotein cholesterol; SD = standard deviation

Prescribing pattern

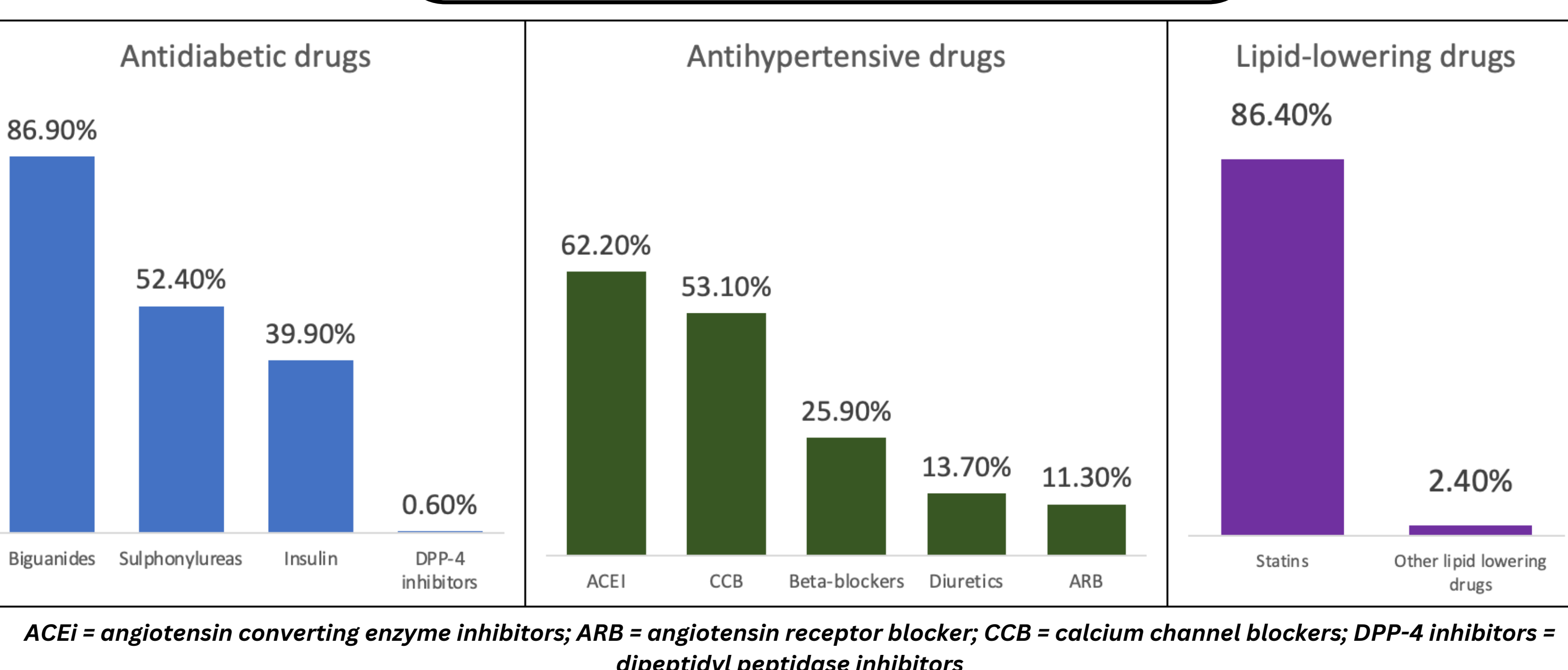
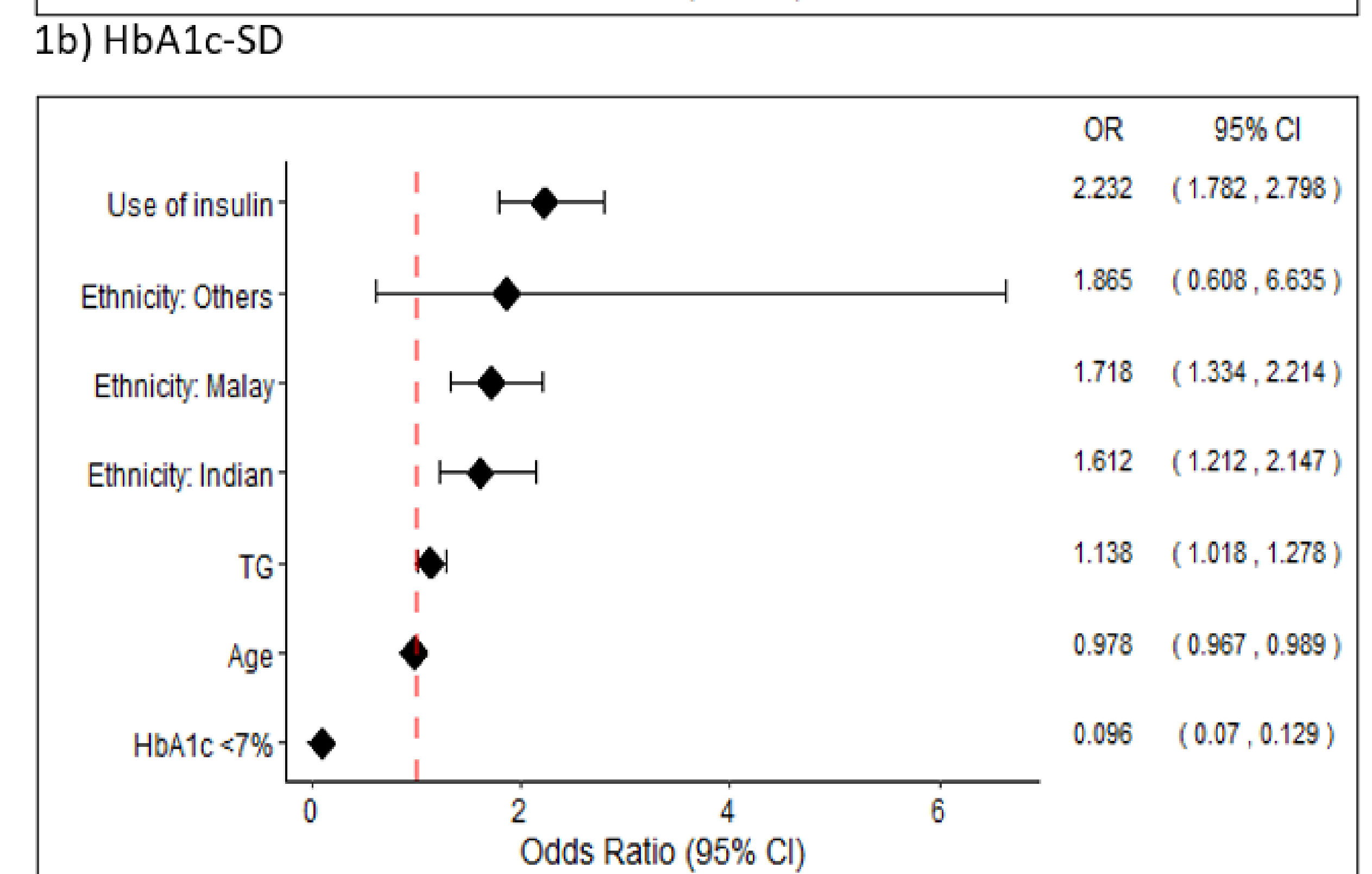
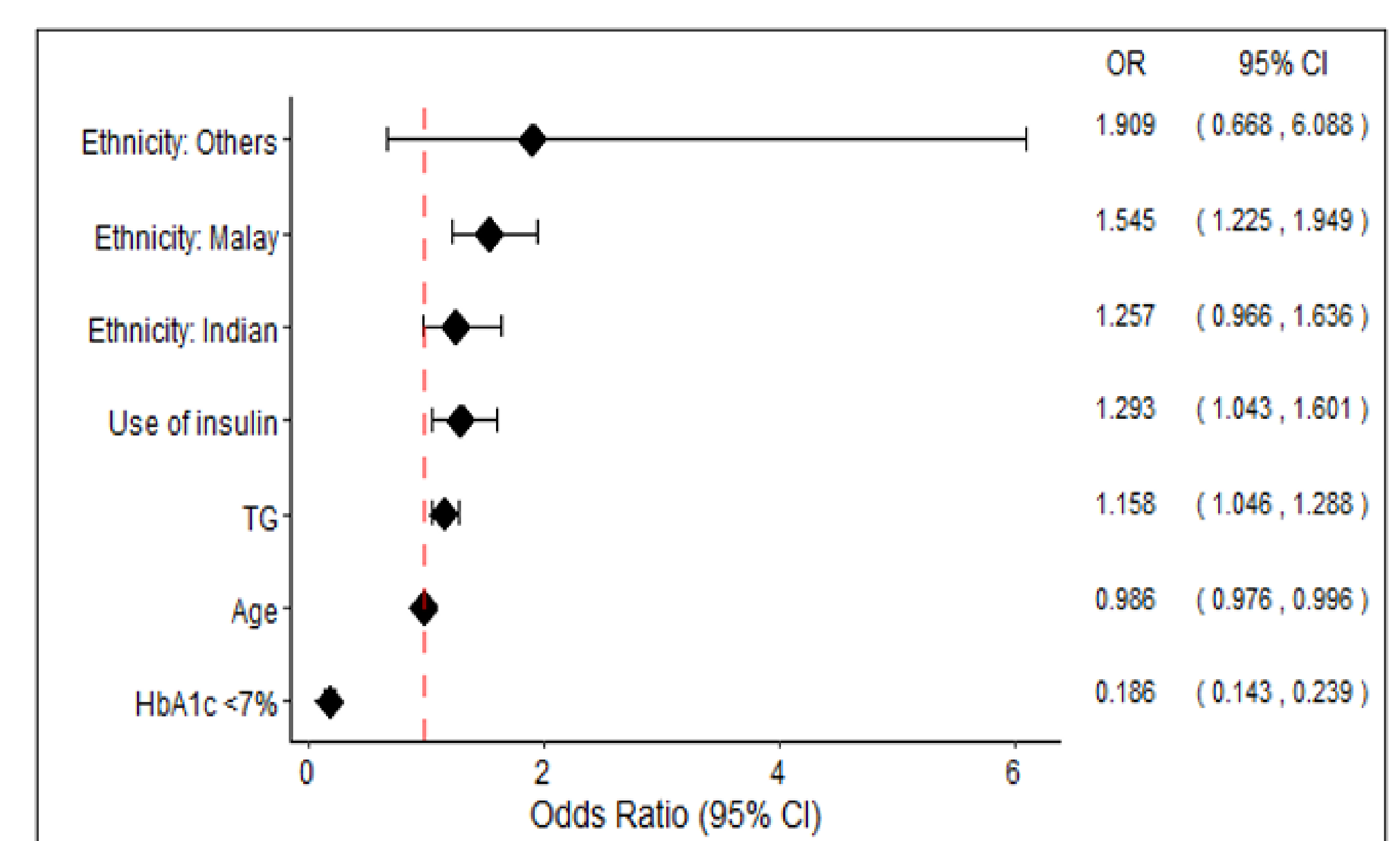


Figure 1 Forest plots of multiple logistic regression for HbA1c-CV and HbA1c-SD



*Complete case analyses were performed, with n=1938

- HbA1c-CV was divided into high and low based on the cut-off point of 9.16.
- HbA1c-SD was divided into high and low based on the cut-off point of 0.75.
- Results showed higher HbA1c-CV among Malay, Indian, and others ethnicities compared to Chinese. Insulin use and higher triglyceride levels demonstrates positive associations with increased HbA1c-CV. In comparison, older patients and those who had good HbA1c control had lower HbA1c-CV.
- HbA1c-SD model had similar results to HbA1c-CV.
- High HbA1c variability was found to be associated with younger age, which is a trend seen in previous studies (4,5). Previous studies also showed that Malays and Indians have worse mean HbA1c level or HbA1c control, when compared to Chinese (7).
- Insulin is known to cause hypoglycaemia, explaining the high HbA1c-SD. Besides, a positive association was found between triglyceride level and HbA1c variability, but the mechanism between triglyceride and glucose metabolism is still debatable as hypertriglyceridemia may be a consequence of impaired glucose metabolism or the one causing it (8,9).

Conclusion

- By identifying the factors associated with HbA1c variability, clinicians can either closely monitor the patients, prescribe drugs that will minimize variability, or educate patients on self-care activities that reduce the variation.
- HbA1c variability will not require additional laboratory test, it can be considered to be an additional measure in diabetes management.

Acknowledgements

The authors would like to thank the Director General of Health Malaysia for the permission to publish this paper. We would also like to thank the data custodian from Family Health Development Division, Ministry of Health.

References

1. Institute for Public Health. National Health and Morbidity Survey (NHMS) 2019: Non-communicable diseases, healthcare demand, and health literacy - Key Findings. Institute for Public Health; 2020.
2. Mo Y, Zhou J, Ma X, Zhu W, Zhang L, Li J, et al. Haemoglobin A1c variability as an independent correlate of atherosclerosis and cardiovascular disease in Chinese type 2 diabetes. *Diab Vasc Dis Res*. 2018 Sep 1;15(5):402-8.
3. Yang CY, Su PF, Hung JY, Ou HT, Kuo S. Comparative predictive ability of visit-to-visit HbA1c variability measures for microvascular disease risk in type 2 diabetes. *Cardiovasc Diabetol*. 2020 Jul 6;19(1):105.
4. Akseelrod D, Friger M, Biderman A. HbA1c variability among type 2 diabetic patients: a retrospective cohort study. *Diabetol Metab Syndr*. 2021 Sep 18;13(1):101.
5. Noyes JD, Soto-Pedre E, Donnelly LA, Pearson ER. Characteristics of people with high visit-to-visit glycaemic variability in Type 2 diabetes. *Diabet Med J Br Diabet Assoc*. 2018 Feb;35(2):262-9.
6. Mellergård E, Johnsson P, Eek F. Sociodemographic factors associated with HbA1c variability in type 2 diabetes: a prospective exploratory cohort study. *BMC Endocr Disord*. 2020 Jul 8;20(1):102.
7. Hong CY, Chia KS, Hughes K, Ling SL. Ethnic differences among Chinese, Malay and Indian patients with type 2 diabetes mellitus in Singapore. *Singapore Med J*. 2004 Apr;45(4):154-60.
8. Parhofer KG. Interaction between Glucose and Lipid Metabolism: More than Diabetic Dyslipidemia. *Diabetes Metab J*. 2015 Oct;39(5):353-62.
9. Boden G, Laakso M. Lipids and Glucose in Type 2 Diabetes: What is the cause and effect? *Diabetes Care*. 2004 Sep 1;27(9):2253-9.