

CORRELATION BETWEEN LIPID PROFILE AND HBA1C IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AT KLINIK KESIHATAN KUALA LUMPUR

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Abstract: Type 2 Diabetes Mellitus (T2DM) is an endocrinological disorder which is associated with hyperglycemia characterized by both insulin resistancy and insulin deficiency. Abnormality in lipid profile leads to cardiovascular risks. Elevation of total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL) and decrease in high density lipoprotein (HDL) are the characteristics of abnormality in lipid profile. **Methods:** This analytical research design with approach of cross sectional has been done in Non-Communicable Disease (NCD) Unit, Diabetic Clinic, Klinik Kesehatan Kuala Lumpur from January to October 2020. Data was taken from medical records of patients and those with incomplete data were excluded from this study. Based on the findings from Klinik Kesehatan Kuala Lumpur a total of 121 samples were collected and all the samples are been used in this study for better results. **Results:** It is found that there is a correlation between high total cholesterol level with high level of HbA1c, where 91.2% of those have high level of cholesterol also have high level of HbA1c ($r=0.331$; $p=0.001$). There is significant correlation between high level of triglyceride and low level of HDL with high level of HbA1c. Around 87.3% of patients have high level of triglyceride also have a high level of HbA1c ($r=0.259$; $p=0.014$). In addition, approximately 89.7% of patients who have low level of HDL also have a high level of HbA1c ($r=0.202$; $p=0.037$). **Conclusion:** There is correlation between lipid profile and HbA1c in patients with T2DM

Keywords: Lipid profile, HbA1c, Type 2 Diabetes Mellitus patients, Malaysia.

1. INTRODUCTION

Diabetes is prone to be known as the life-long disease that affects the way human bodies handle glucose. According to National Institute of Diabetes and Digestive and Kidney Disease (NIDDK), pancreas makes a hormone called insulin. Insulin typically allows cells to turn glucose from food consumed into energy. Diabetes mellitus (DM) is a metabolic disease identified by high levels of blood glucose caused by the decrease in insulin secretion, insulin action, or both. This disease is a severe health problem because it causes many complications both acute and chronic in almost all organs of the body. Most DM patients die because of kidney failure, heart disease, stroke, or infection.^{1,2}

In accordance to the NIDDK, a hemoglobin A1c test also known as (HbA1c) test is been used widely to measure the amount of blood glucose which is the glucose attached to hemoglobin. Hemoglobin is a segment of the red blood cell which functions by carrying oxygen from lungs to the rest of the body. A HbA1c test shows what is the average amount of glucose attached to hemoglobin for the past three months.¹¹ The reading obtained is for the recent three months because that is the normal range of how long a red blood cell lives in the human body.³ The Abbreviated Report of WHO Consultation, entitled the use of glycated hemoglobin (HbA1c) in diagnosing of diabetes mellitus has stated that the hemoglobin A1C assay has become the gold-standard measurement of chronic glycemia for over the years.³

In type 2 diabetes, hypercholesterolemia can interfere with the function of endothelium by increasing the yield of free radicals oxygen. These radicals deactivate the nitric oxide, namely the main relaxing endothelial factor. If chronic occurs, lipoproteins accumulate in the intima layer at the site of endothelial and the permeability increased. Exposure to free radicals in arterial walls of the endothelial cells causes oxidation of LDL cholesterol, which plays an accelerating role in the formation of atheromatous plaque.¹¹ The oxidation of LDL cholesterol is strengthened by low HDL levels in type 2 diabetes mellitus together with lack of estrogen in some particular cases.⁴

Thereby, the main reason for the conduction of this study is to understand the relationship between lipid profile and HbA1c in type 2 diabetics at Klinik Kesihatan Kuala Lumpur. Another reason is to understand the characteristics of these patients and what are the complications or metabolic conditions faced by them.

2. MATERIALS AND METHODS

This study uses an analytical research design with approach of cross sectional which aims to determine the correlation between lipid profile and HbA1c in patients with type 2 diabetes at Klinik Kesihatan Kuala Lumpur from January until October 2020 according to those aged more than or equivalent to 25 years old, gender, clinical manifestation, lab tests, treatment and outcomes based on Medical records of the patients which is used as the secondary data for this research. The advantage of this study is usually takes short time for completion and its applicability to rare diseases.

The protocol of this research has been divided into three main component which is the preparation stage, implementation stage and analysis stage. For the preparation stage, research proposal is prepared together with recommendation letter and sent to Research & Development Department for collecting data. Letter is further sent for approval of ethical clearance. Upon filing ethical clearance the preparation is preceded for approval from Medical Officer in Charge (MOIC) of Klinik Kesihatan Kuala Lumpur. Implementation stage is conducted upon approval from MOIC of Klinik Kesihatan Kuala Lumpur to carry out the research. In this stage, the medical records of patients with type 2 diabetes mellitus is taken down based on the criteria and analyzed of sample.

The univariate analysis is only a descriptive study in this study that describes the frequency distribution, mean, median and interquartile range of gender, race, HbA1c, TC, TG, HDL, LDL. To test the normality of distribution Kolmogorov Smirnov is used in this study. Bivariate analysis is done using the Chi Square test (parametric test) if eligible. Chi Square test and r are used to determine the significance and strength of relationship between variables. P value <0.05 declared statistically significant. Statistical package of the Social Science Software version 16.0 (SPSS Inc., Chicago, IL., USA) will be used to analyze the data which will be further presented in table and narrative form. This research has received ethical eligibility permission from the Research Ethics Commission (KEP) of the Faculty of Medicine, Udayana University with letter number 453/UN14.2.2.VII.14 / LT / 2020.

3. RESULTS AND DISCUSSION

According to demographic characteristics, it can be noted that patients' age ranged from 25 years old to 86 years old. The distribution normality was assessed by using Kolmogorov Smirnov test, with the result that age is normally distributed ($p>0.05$), therefore the data will be shown in the form of mean + standard deviation. It is found that the age average is 49.61 + 14.2 years old. The majority of patients are Malays which is accounted for 67.8%, followed by Indian (19.8%) and Chinese (12.4%). In accordance to gender, there is only a slight difference in between male and female which are accounted for 47.1% and 52.9% respectively. Details data can be seen in table 1.

Table 1: Demographic Characteristics of Samples

Demographics	F (%)
Age (Mean ± SD)	49.61 ± 14.2 years old
• Adult (25-60 years old)	89 (73.6)
• Elderly (>60 years old)	32 (26.4)
Races	
• Malay	82 (67.8)
• Indian	24 (19.8)
• Chinese	15 (12.4)
Gender	
• Male	57 (47.1)
• Female	64 (52.9)

SD: standard deviation; F: frequency

HbA1c Characteristics of Samples

HbA1c is used as a glycemic control among diabetic patients. In this study, HbA1c ranged from 6.50% to 15%, with the mean of 8.86 + 2.1 %. The distribution of data was analyzed using Kolmogorov Smirnov test and found that HbA1c data is not normally distributed ($p < 0.05$). HbA1c is then classified based on the reasonable target for diabetic patients which is below 7%. It is noteworthy to see that the vast majority of patients have a high HbA1c level (84.3%) whereas the rest have the level within the target value (15.7%). Complete details can be seen in table 2.

Table 2: HbA1c Characteristics of Samples

Demographics	F (%)
HbA1c (Median; IQR)	8.30; 3.05
• Within Target (<7%)	19 (15.7)
• Above Target (>7%)	102 (84.3)

F: frequency

Lipid Profile Characteristics of Samples

The total cholesterol ranged from 110-305 mg/dL with the average of 214.16 + 29.2 mg/dL. There are 75.2% of patients who have a considerably high total cholesterol level. Triglyceride ranged from 100-558 mg/dL with the average of 336.18 + 140.8 mg/dL. The vast majority of the patients have a high level of triglyceride, which is accounted for 90.9%. For HDL, the value is ranged from 23 to 60 mg/dL with the average of 38.43 + 9.7 mg/dL. More than a half of participants (64.5%) have a low level of HDL which is below 40 mg/dl. The LDL is ranged from 33 to 220 mg/dL with the average of 142.3 + 30.8 mg/dL. There are 91.7% of patients who have a high level of LDL. Complete data can be seen in Table 3.

Table 3: Lipid Profile Characteristics of Samples

Demographics	F (%)
Total Cholesterol (Median; IQR)	209.0; 32.0
• Normal (120-200 mg/dL)	30 (24.8)
• High (>200 mg/dL)	91 (75.2)
Triglyceride (Median; IQR)	359.0; 285.0
• Normal (\leq 150 mg/dL)	11 (9.1)
• High (>150 mg/dL)	110 (90.9)
HDL (Median; IQR)	39.0; 15.0
• Normal (\geq40 mg/dL)	43 (35.5)
• Low (<40 mg/dL)	78 (64.5)
LDL (Mean \pm SD)	142.28 \pm 30.79
• Normal (\leq 100 mg/dL)	10 (8.3)
• High (>100 mg/dL)	111 (91.7)

F: frequency; IQR: interquartile range

Correlation between Lipid Profile and Hb1Ac

The correlation between lipid profile and HbA1c level is assessed using chi-square test in the form of 2x2 cross-tabulation data. It is found that there is a correlation between high total cholesterol level with high level of HbA1c, where 91.2% of those who have a high level of cholesterol also have a high level of HbA1c ($r=0.331$; $p=0.001$). There are also significant correlations between high level of triglyceride and low level of HDL with high level of HbA1c. Around 87.3% of patients who have high level of triglyceride also have a high level of HbA1c ($r=0.259$; $p=0.014$). In addition, approximately 89.7% of patients who have low level of HDL also have a high level of HbA1c ($r=0.202$; $p=0.037$). Nevertheless, there is a very slight weak significant correlation found between high level of LDL and high level of HbA1c, in spite of high percentage of patients who have high level of LDL and high level of HbA1c at the same time. The complete data can be seen in Table 4.

Table 4: Correlation between Lipid Profile and HbA1c

Lipid Profile	HbA1c Level		r	P
	Within Target	Above Target		
Total Cholesterol				
• Normal	11 (36.7)	19 (63.3)	0.331	0.001*
• High	8 (8.8)	83 (91.2)		
Triglyceride				
• Normal	5 (45.5)	6 (54.5)	0.259	0.014*
• High	14 (12.7)	95 (87.3)		
HDL				
• Normal	11 (25.6)	32 (74.4)	0.202	0.037*
• Low	8 (10.3)	70 (89.7)		
LDL				
• Normal	4 (40.0)	6 (60.0)	0.200	0.05
• High	15 (13.5)	96 (86.5)		

4. DISCUSSIONS

In this study, particularly, the correlation between lipid profile and HbA1c in patients with type 2 diabetes mellitus is been evaluated. According to the demographic characteristics results obtained, patients are been divided into 2 groups which consist of adults age ranged (25-60 years old) and elderly (>60 years old) with an age average of 49.61 ± 14.2 years old. Next, there are 3 major race in Malaysia consists of Malay, Indian and Chinese. From this study it can be seen that majority of type 2 diabetics are of Malay race (67.8%) followed by Indian (19.8%) and finally Chinese (12.4%). In accordance to a randomized study conducted at a tertiary care hospital in Malaysia, HbA1c of diabetes mellitus and ethnicity showed no significant association with lipid profile values.^{6,7}

Some of the previous studies conducted in Malaysia has revealed mixed results. Some showed either no or little role of the HbA1c in determining the risk of dyslipidemia and cardiovascular disease amongst different races.⁷ While on the other hand, others demonstrated a positive correlation of HbA1c with CVD and various ethnicity in Malaysia. Previously, Davis et al and Zhang et al⁸ has found out the importance of ethnic differences in Malaysia in determining the lipid profile of type 2 diabetics. Their results has shown a distinct pattern of lipid profile amongst various ethnicity.

Now having a look from the gender perspective, out of 121 patients that has fulfilled the inclusion and exclusion criteria, there is only a slight difference observed between the male and female which is 57 (47.1%) and 64 (52.9%) respectively. A study conducted by Julianto et al⁹ also showed a similar result where it was stated that most of the type 2 diabetics were female too. On another study by Wexler et al¹² has been reported that a significant correlation between HbA1c and TC, HDL-C and LDL-C in female diabetics, which suggested the importance of proper management of diabetes mellitus in order to take control of diseases like Dyslipidemia and Hypercholesterolemia.

According to a recent study by Diabetes Care and Control Trial (DCCT), HbA1c is characterized as the gold standard of glycemic control. In this study, HbA1c is ranged from 6.5% to 15% with an average mean of 8.30.¹³ Therefore, in this study HbA1c is been classified in 2 different categories which is within target (<7.0%) and above target ($\geq 7.0\%$). It was clearly noted down that majority of the type 2 diabetes patients have an increased HbA1c level 102 (84.3%) whereas the rest are still within target value 19 (15.7%). These findings are consistent with some previous studies. According to a similar study conducted by Hussain et al¹⁰, out of 401 (175 males; 226 females) patients who fulfilled the inclusion and exclusion criteria 66 patients has HbA1c <7.0% and the majority of patients has HbA1c $\geq 7.0\%$ (335 patients).

The results obtained in this study shows that those with HbA1c greater than 7.0% exhibit a significant increase in TC, HDL-C and TG comparative to those with HbA1c within target. This results is in agreement with the findings of several other investigations which reported significant correlation between HbA1c and lipid profile. The diabetes mellitus patients with poor glycemic control exhibit a significant rise in cholesterol and TG and decrease in HDL without any significant alteration in LDL.¹¹

In my opinion, this dissimilarity in this study compared other studies could be due to the inaccuracy of sample size and with that being said, more studies with larger sample size should be conducted at multiple places to evaluate and obtain better results with stronger statistical power. Also, the dissimilarity of the results in this study compared to some other studies might also be due to the geographical regions, races and major difference in ethnical groups.

Research Limitations

This study suffered from the following limitations; first due to the current pandemic situation, it was difficult to access patients medical records in hospitals. Second, limitations in accessing to data in this study might have affected the statistical power of each variable.

5. CONCLUSION

The common characteristics of patients with T2DM according to the demographic characteristics results obtained, patients are been divided into 2 groups which consist of adults age ranged (25-60 years old) and elderly (>60 years old) with an age average of 49.61±14.2 years old. Next, there are 3 major race in Malaysia consists of Malay, Indian and Chinese. From this study it can be seen that majority of type 2 diabetics are of Malay race (67.8%) followed by Indian (19.8%) and finally Chinese (12.4%). Between the male and female which is 57 (47.1%) and 64 (52.9%) respectively it shows that female diabetics are higher than males. Secondly, there is a significant difference in lipid profile between T2DM patients with normal and above target HbA1c as seen in the results and discussion of this study. For the p values of correlation between Lipid Profile and Hb1Ac, TC and HbA1C is (p=0.001), followed by TG and HbA1c (p=0.014), HDL and HbA1c is (p=0.037), LDL and HbA1c is (p=0.05). This study adds on to the existing literature suggesting that lipid profile has a strong correlation with HbA1c and it can used as an indicator for cardiovascular diseases like Hypercholesterolemia, Hypertriglyceridemia and other complications in T2DM.

6. RECOMMENDATION

More comprehensive management is needed from both healthcare workers as well as patients so that Hba1c levels and lipid profile are controlled and complications are maximum prevented. It is advised to Type 2 Diabetics to always be aware of their glycemic control and lipid profile range. Patients are advised to get regular check-ups to the hospital in order to avoid any unnecessary health related implications. It is always important to educate themselves on the risk factors and complications of above target HbA1c and abnormal lipid profile. Just by maintaining a proper diet, exercising, and having the right body mass index type 2 diabetes can be controlled. With the incidence of diabetes on a constant rise around the world, educating, routinely monitoring, and evaluation of HbA1c and lipid profile helps in the reduction of causing microvascular, macrovascular and other complications.

For future researches it is highly suggested to explore deeper into the correlation between lipid profile and HbA1c in patients with type 2 diabetes mellitus that were not discussed in this research. For example, in the demographic features of cases and controls, other parameters that can be included are body mass index (BMI), waist circumference, upper arm circumference, systolic blood pressure (SBP) and diastolic blood pressure (DBP). This will definitely be beneficial and helpful to the community and country as well. Therefore, it is important for the community to increase their knowledge in order to prevent diabetes and its related health complications.

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