International Journal of Biomedical Research
ISSN: 0976-9633 (Online); 2455-0566 (Print)
Journal DOI: https://dx.doi.org/10.7439/ijbr
CODEN: IJBRFA

Original Research Article

Glycated hemoglobin: A surrogate marker of coronary artery diseases?

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***Article History:**
Received: 17/03/2017
Revised: 31/03/2017
Accepted: 31/03/2017
DOI: https://dx.doi.org/10.7439/ijbr.v8i4.4043

Abstract

Background: Diabetes mellitus is a global epidemic defined by elevated glycated hemoglobin (HbA_{1c}). The symbiotic relationship between diabetes and dyslipidemia has been studied and glycated hemoglobin has been projected as a potential marker for coronary artery diseases.
Aim: To study the correlation between the HbA_{1c} and the lipid ratios / individual lipids
Methods: The data was collected from 90 patients of type 2 Diabetes Mellitus over a period of 6 months, after an informed written consent. The study subjects were divided according to the HbA_{1c} values into three groups - Group A: HbA_{1c} < 7%, Group B: HbA_{1c}= 7-10%, Group C: HbA_{1c} >10 %. The lipid profiles of the patients after a minimum of 8 hours of fasting were noted. The values of the lipid ratios and the individual lipids were mapped against the HbA_{1c} values of each group. The correlation between the glycated hemoglobin and the lipid profile was analysed.
Results: The maximum numbers of patients (30%) were in the 6th decade of life. Among the study subjects, 39 patients (43.33%) were females and 51 patients (56.66%) were males. Group B had the majority of patients (44.4%) followed by group A. There was a positive correlation between HbA_{1c} and triglycerides (p=0.04) and a negative correlation between HbA_{1c} and HDL (p=0.003). There was a positive correlation between HbA_{1c} and LDL/HDL (p=0.022), TG/HDL (p=0.008) and TC/HDL (p=0.007). Thus the TC/HDL ratio was most impaired by a rise in HbA_{1c} when compared with other lipid ratios.
Conclusion: There is a significant positive correlation between HbA_{1c} and lipid ratios. Lipid ratios in turn are important predictors of CAD. Hence HbA_{1c} can be used to predict dyslipidemia and CAD in patients with Type 2 diabetes mellitus and can be used as a surrogate marker for the same.
Keywords: Glycated hemoglobin, lipid profile, dyslipidemia, coronary artery disease.

1. Introduction

Diabetes Mellitus has become a global epidemic, affecting the developing and the developed countries alike. It has been predicted that by the year 2030, the total number of patients suffering from diabetes would be 439 million, as opposed to 285 million in the year 2010.[1]

The measurement of the glycated hemoglobin [HbA_{1c}] has become an indispensable part of the criteria for the diagnosis of diabetes mellitus. As per the American Diabetes Association, a glycated hemoglobin value of more than or equal to 6.5% is used to identify the individuals with diabetes mellitus [2].

Patients with diabetes mellitus are at an increased risk for developing Coronary Artery Diseases [CAD]. It is the most common cause for death in individuals with diabetes.[3]

Dyslipidemia is another independent risk factor for CAD. When the two co – exist, one disease process augments the other, leading to the lesser known condition called diabetes lipidus[4].

Thus, according to the current recommendations, a screening lipid profile has to be performed at the time of diagnosis of type 2 diabetes mellitus and statins should be started if required [5].

An objective evidence of this symbiotic relationship could be obtained by studying the correlation between glycated hemoglobin and lipids. A study conducted at the University of Pennsylvania has shown that the lipid ratio is a superior indicator of the risk for CAD when compared with the individual lipids [6].

Thus, the study aims to correlate the HbA_{1c} and the lipid ratios in individuals with type 2 diabetes mellitus and hence project HbA1c as a marker of CAD.

1.1 Objectives of the study

- To study the glycated hemoglobin and the lipid profile of patients with type 2 Diabetes Mellitus.
- To study the correlation between the HbA_{1c} and the lipid ratios / individual lipids.

2. Material and methods

2.1 Source of data

The data was collected from 90 patients of type 2 Diabetes Mellitus who reported to Father Muller Medical College Hospital, Mangalore.

2.2 Method of collection of data

Study design: Observational Analytical Study

Period of study: 6 months

A study sample comprising ninety subjects fulfilling the inclusion and the exclusion criteria was included in the study using the purposive sampling technique after an informed written consent.

The following information regarding the patient was documented- name, age and the hospital registration number. Type 2 Diabetes Mellitus was defined as per the American Diabetes Association Criteria [HbA_{1c} > 6.5 %] . The study subjects were divided according to the HbA_{1c} values into three groups: - Group A : HbA_{1c} < 7%,Group B : HbA_{1c}=7-10 %, Group C : HbA_{1c} >10 %.

The lipid profiles of the patients after a minimum of 8 hours of fasting were noted. The values of the lipid ratios [TG/HDL, TC/HDL, LDL/HDL] and the individual lipids [TG, TC, HDL, LDL] were mapped against the HbA_{1c} values of each group. Where TC = total cholesterol, HDL = high density lipoprotein, LDL =low density lipoprotein and TG= triglycerides. The correlation between the glycated hemoglobin and the lipid profile was analysed.

2.2 Inclusion criteria

- Age above 18 years
- HbA_{1c} > 6.5%

2.3 Exclusion criteria

- Patients with hyperglycemia due to non diabetic causes (drug-induced, stress related, hypercortisolemia, etc.)
- Patients with a prior diagnosis of Type 1 Diabetes Mellitus
- Patients suffering from life threatening illnesses and those admitted in the critical care units
- Patients receiving lipid controlling drugs in the past 3 months before inclusion into the study

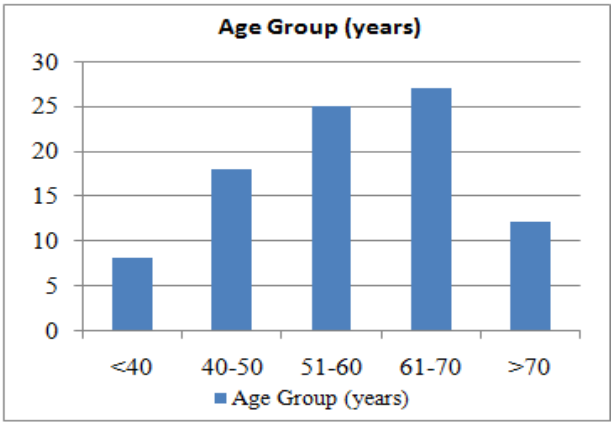
2.4 Statistical analysis

The collected data was analyzed by mean, standard deviation and ANOVA methods.

3. Results

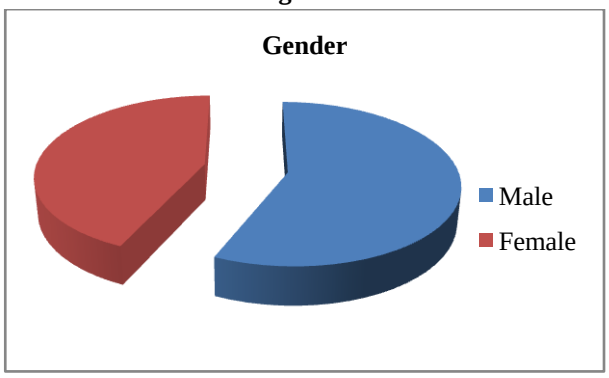
A total number of 90 patients were found to be suitable for the analysis. The maximum number of patients [30%] was in the 6th decade of life. [Figure 1]

Figure 1: Age Groups (Years)



Among the study subjects, 39 patients [43.33%] were females and 51 patients [56.66%] were males [Figure 2].

Figure 2: Gender



The patients were divided into three groups based on the HbA_{1c} values. Group B with HbA_{1c} values between 7 to 10 % had the majority of patients [44.4%] followed by group A [28.9%]. [Table 1]

Table 1: Group

	Frequency	Percent
Group A	26	28.9
Group B	40	44.4
Group C	24	26.7
Total	90	100.0

Table 2: Shows the mean, the maximum and the minimum values of the parameters under study

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles		
						25th	50th (Median)	75th
Cholesterol	90	170.58	58.130	74	336	127.75	160.50	208.50
Triglycerides	90	163.04	106.097	55	683	99.25	136.50	197.00
HDL	90	29.99	15.504	2	79	18.75	30.00	40.00
LDL	90	107.40	55.479	2	262	69.75	105	140.00
HBA_{1C}	90	8.720	2.3493	6.5	18.1	6.900	7.800	10.600

The correlation between the HbA_{1c} and the individual blood lipids/ lipid ratios is demonstrated below [Tables 3 and 4]. There was a positive correlation between HbA_{1c} and triglycerides [p=0.04] and a negative correlation between HbA_{1c} and HDL [p=0.003].

Table 3: The correlation between the HbA_{1c} and the individual blood lipids/ lipid ratios

		HBA_{1C}	HDL	LDL	TG/HDL	TC/HDL	LDL/HDL	Cholesterol	Triglycerides
HBA_{1C}	**Pearson Correlation**	1	-0.305	-0.040	0.278	0.280	0.241	-0.097	0.217
	p		0.003	0.711	0.008	0.007	0.022	0.362	0.040
HDL	**Pearson Correlation**	-0.305	1	0.273	-0.500	-0.613	-0.420	0.355	-0.302
	p	0.003		0.009	0	0	0	0.001	0.004
LDL	**Pearson Correlation**	0.040	0.273	1	-0.424	-0.267	0.553	0.762	0.086
	p	0.711	0.009		0	0.011	0	0	0.423
TG/HDL	**Pearson Correlation**	0.278	-0.500	-0.424	1	0.896	-0.110	-0.168	0.663
	p	0.008	0	0		0	0.303	0.113	0
TC/HDL	**Pearson Correlation**	0.280	-0.613	0.267	0.896	1	0.133	-0.055	0.492
	p	0.007	0	0.011	0		0.210	0.606	0
LDL/HDL	**Pearson Correlation**	0.241	-0.420	-0.553	-0.110	0.133	1	0.127	0.053
	p	0.022	0	0	.0303	0.210		0.233	0.617
Cholesterol	**Pearson Correlation**	0.097	0.355	0.762	-0.168	-0.055	0.127	1	0.209
	p	0.362	0.001	0	0.113	0.606	0.233		0.048
Triglycerides	**Pearson Correlation**	0.217	-0.302	0.086	0.663	0.492	-0.053	0.209	1
	p	0.040	0.004	0.423	0	0	0.617	0.048	

There was a positive correlation between HbA_{1c} and LDL/HDL [p=0.022], TG/HDL [p=0.008] and TC/HDL [p=0.007]. Thus the TC/HDL ratio was most impaired by a rise in HbA_{1c} when compared with other lipid ratios.

Table 4: The correlation between the HbA_{1c} and the individual blood lipids/ lipid ratios

	Group	Mean	Std. Deviation	Median	25th percentile	75th percentile	Kruskall wallis test	
							Value	p value
TG/HDL	Group A	7.343	16.659	3.167	2.166	5.030	19.142	HS 0
	Group B	5.845	4.031	5.023	3.592	6.563		
	Group C	23.987	36.700	11.368	4.591	19.178		
TC/HDL	Group A	6.008	7.098	4.594	3.304	5.610	15.940	HS 0
	Group B	6.517	1.884	6.984	5.192	7.697		
	Group C	12.576	10.865	9.000	4.771	16.066		
LDL/HDL	Group A	2.553	1.114	2.6116	1.6765	3.6600	13.601	HS 0.001
	Group B	4.146	1.371	4.2408	3.0000	5.2553		
	Group C	6.298	5.166	4.2258	1.9750	10.0000		

4. Discussion

Diabetes mellitus and dyslipidemia are complementary disease processes. They interact with each other, to accelerate atherogenesis and cause coronary artery diseases. [7-9]

This has lead to the coining of the term diabetic dyslipidemia / Diabetes Lipidus. It is characterised by an elevation in the triglyceride rich lipoproteins and a decrease in the serum HDL levels. LDL is converted into smaller lipoproteins that are more atherogenic. These changes precede the onset of type 2 diabetes mellitus by many years.[10-12] Kelly *et al* have proven in their study that oxidised LDL was significantly related to an increase in the insulin resistance. [13]

In our study, we found a positive correlation between HbA_{1c} and all the three lipid ratios. The strongest correlation was between HbA_{1c} and TC/HDL [p=0.007] followed by TG/HDL [p=0.008] and LDL/HDL [p=0.022]. This in agreement with a study conducted in China by Yan *et al*. However, the strongest correlation in that study was between HbA_{1c} and LDL/HDL [p=0.003] followed by TC/HDL [p=0.039] and TG/HDL [p=0.301][14].

Among the individual lipids, there was a positive relation between triglycerides and HbA1c [p=0.04] and a

negative correlation between HDL and HbA1c [p=0.003]. However, we could not find a positive relation with TC and LDL unlike other studies [15-17]. Hence the concordance between HbA_{1c} and lipid ratios was better than with individual lipids.

The lipid ratio is a significant predictor of CAD. A study conducted by Sathiya *et al* showed increased LDL/HDL [p<0.001] and TC/HDL [p<0.001] in CAD patients [18]. Another study conducted in Washington demonstrated TC/HDL as a predictor of CAD in women [19]. Lemieux *et al*, in their research concluded that variations in TC/HDL were more closely related to the risk of having a CAD than LDL/HDL [20].

Thus, this study has indirectly drawn a correlation between glycated haemoglobin and CAD. This is further supported by a study by Ikeda *et al* which states that HbA_{1c} is associated with the severity of coronary artery lesions [21]. Another study in China concluded that chronic hyperglycemia, predicted by the HbA1c values was associated with CAD [22].

This study also reiterates the necessity to actively screen for dyslipidemia in patients with type 2 diabetes mellitus. Aggressive treatment of diabetic dyslipidemia will reduce the risk of coronary artery diseases in diabetics. This has been proven in a Collaborative Atorvastatin Diabetes Study [CARDS]. The study even suggests that stains should be considered in patients with lower LDL [23]. The 2016 ADA guidelines suggest that moderate intensity statins should be started in diabetics between 40-75 years even when they have no risk factors for CAD.

This research was conducted over a 6 month period. Hence, the subjects under the study could not be followed up to detect CAD at a later age group. This study could be further developed by giving it a prospective course.

5. Conclusion

There is a significant positive correlation between HbA1c and lipid ratios. Lipid ratios in turn are important predictors of CAD. Hence HbA1c can be used to predict dyslipidemia and CAD in patients with Type 2 diabetes mellitus and may be used as a surrogate marker for the same.

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