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RELATIONSHIP BETWEEN GLYCOSYLATED HEMOGLOBIN AND LIPID METABOLISM IN PATIENTS WITH TYPE 2 DIABETES

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ABSTRACT

Diabetic patients with accompanied dislipidemia are soft targets of cardiovascular deaths. An early intervention to normalize plasmatic lipids has been shown to reduce cardiovascular complication and mortality at type 2 diabetic patients. Glicated hemoglobin (HbA1c) is a used marker for long term glycemic control. His investigation is an attempt to evaluate the diagnostic value of HbA1c in predicting ddiabetic dislipidemia. Venous blood was collected from 112 type 2 diabetic patients age 35 – 75 years, 62 males and 50 females. The sera were analysed for HbA1c, basal blood glucose, total cholesterol, tryglicerides, high density lipoprotein cholesterol (HDL cholesterol) and low density lipoprotein cholesterol (LDL cholesterol). The levels of HbA1c did not differ significantly between males and females. HbA1c showed direct and significant correlation with cholesterol, triglicerides and LDL cholesterol, and revers correlation with HDL cholesterol. Female diabetic patients had significantly higher levels of serum cholesterol and HDL cholesterol compared to males. They were no significant differences in triglicerides in LDL between the two genders. There was a significant increase in triglicerides in the patients of both genders with impaired glicemic control. Both males and females patients with worse glicemic control (HbA1c > 9%) had significantly high cholesterol and LDL levels. Serum HDL showed a significant and inverse relationship with uncontrolled hiperglicemia in females but not in males. These findings clearly suggest that HbA1c can provide valuable suplimentary information about the extent of circulating lipids besides in its primary role in monitoring long term glycemic control. Further studies are warranted to reinforce the potential of HbA1c as a biomarker for screening of high risk diabetic patients.

Key words: type 2 diabetes, dyslipidemia, glycemic control, HbA1c

PATIENTS AND METHODS

Study comprised a total of 112 type 2 diabetic patients who were examined at a private laboratory, in a national study of HbA1c in type 2 diabetic patients

There were 62 males and 50 females. The age of patients ranges between 30 and 80 years. All the patients were categorized into four age groups : < 50; 50-60; 60-70' > 70 years.

Venous blood samples from all the subjects were collected in serum separator tubes.

The sera were analyzed for glycated hemoglobin (HbA1c), fasting blood glucose (FBS), total cholesterol, triglycerides (TS) and high density lipoprotein cholesterol (HDL) using an auto analyzer Hitachy 17

The level of low density lipoprotein cholesterol (LDL) was determined using the formula: LDL = (Cholesterol – TG) / (2,2 HDL). The impact of glycemic control on various parameters was evaluated by categorizing all the patients into 3 categories on the basis of HbA1c levels : HbA1c < 6% (good glycemic control, HbA1c > 6-9% (poor glycemic control) and HbA1c > 9 % (worse glycemic control)

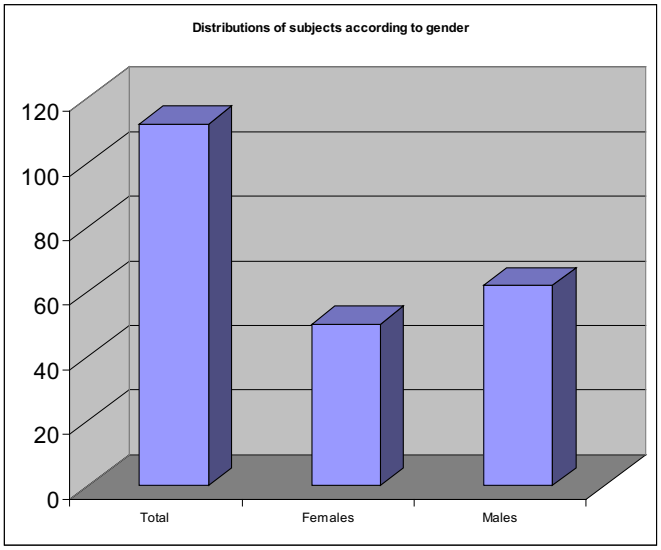
RESULTS

Male and female diabetic patients exhibited similar paterns of glycemic control, depending on three cutoff values of HbA1c (Table 1, Chart 1)

Table 1 : Distribution of subjects according to gender and HbA1c cutoffs

Glycemic Control	HbA1c Criteria	Male		Female		Total subjects	
		Nr	Percentage	Nr	Percentage	Nr	Percentage
Good	<6%	6	10,1	5	10,1	11	10
Poor	>6-9%	31	50,7	25	47,8	56	51
Worse	>9%	25	39,2	20	42,1	45	39
All Subjects	-	62	100	50	100	112	100

Chart 1 : Distribution of subjects according to gender



There was no significant correlation between patient age and HbA1c . A significant correlation was observed between FBG and HbA1c. Also demonstrated direct and significant correlations with cholesterol, triglycerides and LDL and inverse correlation with HDL (Table 2)

Table 2 : Serum biochemistry categorized by patients gender

Parameter	Gender of patients	
	Male (N=62)	Female (N=50)
HbA1c	10,11 +- 0,04%	10,21 +- 0,05%
FBG	12,16 +- 0,04%	13,01 +- 0,14%
Cholesterol	5,8 +- 0,10%	6,2 +- 0,13%
Trigliceride	2,3 +- 0,11%	2,5 +- 0,14%
HDL	0,90 +- 0,01%	1,2 +- 0,09 %
LDL	4,60 +- 0,09%	4,82 +- 0,11%

Although the levels of triglycerides were lower and levels of LDL higher in females than males, these difference were not statistically significant (Table 2)

Diabetic patients with poor (HbA1c > 6-9%) and worse (HbA1c >9%) glycemic control had significantly higher levels of FBG ($p<0,001$) and triglycerides ($P< 0,001$) and significantly lower levels of HDL ($P<0,001$) as compared to patients with good glycemic control (Table 3)

Table 3 : Serum biochemistry categorized by patients glycemic control (HbA1c)

Parameter	HbA1c		
	<6 % (N=11)	>6 - 9 % (N=56)	> 9 % (N=45)
FBG	5,1 +- 1,10%	9,16 +- 1,03%	12,9 +- 1,6%
Cholesterol	5,41 +- 1,2%	5,62+- 10,2%	5,81 +- 1,4%
Triglyceride	1,93 +- 0,06%	2,21 +- 1,03%	2,39 +- 0,16%
HDL	1,10 +- 0,05%	1,01 +- 0,04%	0,92 +- 0,68%
LDL	4,10 +- 0,17%	4,61 +- 0,18%	4,80 +- 0,20%

Both male and female diabetic patients exhibited similar paterns of glycemic control, depending of three cutoff values of HbA1c (Table 1) . Whereas a highly significant correlation was observed between FBG and HbA1c. These was no significant correlation between patient age and HbA1c. Also demonstrated and significant correlations with cholesterol, triglycerides and LDL, and inverse correlations with HDL. (table 4)

Table 4 : Serum biochemistry categorized by patients age

Parameters	Age of patients			
	< 50 years	51 – 60 years	61 – 70 years	> 70 years
HbA1c	8,175 +- 9,09	8,286 +- 0,09	8,260 +- 0,08	8,100 +- 0,14
FBG	9,518 +- 0,28	9,307 – 0,16	9,640 +- 0,17	9,12 +- 0,22
Cholesterol	5,304 +- 0,05	5,300 +- 0,03	5,017 +- 0,05	5,010 +- 0,06
Triglycerides	1,810 +- 0,05	2,166 +- 0,05	1,804 +- 0,36	1,908 +- 0,6
HDL	1,121 +- 0,01	1,130 +- 0,02	1,180 +- 0,02	1,200 +- 0,02
LDL	3,460 +- 0,05	3,381 +- 0,04	3,186 +- 0,04	3,125 +- 0,07

Among the circulating lipids, total cholesterol in HDL cholesterol, where significantly higher in female patients. Although the levels of triglycerides where lower and of LDL higher in female than males, this differences were not statistically significant (table 2)

Alterations in serum biochemical parameters in various age group of patients are shown in table 4 . All the patients had significantly lower FBG (P=0,44) triglycerides (P=0,028), LDL (P=0,01) and cholesterol (P<0,001). However there was no significant difference between HbA1c, (P=0,150) as well as HDL (P=0,128)

Diabetic patients with poor (HbA1c>6-9%) and worse (HbA1c.9%) glycemic control had significantly higher levels of FBG (P<0,001) and triglycerides (P<0,001) and significantly lower levels of HDL (P<0,001) as compared to patients with good glycemic control (HbA1c < 6 %) (Table 4)

There was a significant increase in total cholesterol (P < 0,001) and LDL cholesterol (P<0,001) in diabetic patients with worse glycemic control as compared to the poor glycemic control group (Table 4)

Patients age had no significant impact on glycemic control in both genders. There was a linear relationship between glycemic control and FBG, while both male and female patients with poor and worse glycemic control had significantly higher FBG as compared to patients with good glycemic control.

Female patients with good glycemic control had comparatively higher cholesterol, HDL and LDL as compared to males with the same level of glycemic control

Both male and female patients with worse glycemic control (HbA1c > 9%) possessed significantly high cholesterol as compared to patients of respective gender in having poor glycemic control. There was a linear and significant increase in triglycerides in the patients of both genders with impaired glycemic control . Both males and females with worse glycemic control had significantly high LDL levels. On the other hand, serum HDL, showed a significant and opposite relationship with uncontrolled glycemia and females, but not in males

DISCUSSION

The distribution of subjects according to gender and specific HbA1c cutoffs showed that most of the type 2 diabetic patients experience poor or worse glycemic control, irrespective of the gender (Table 1)

A significant correlation between HbA1c and FBG is an agreement with earlier reports (Ko GT,et colab 1998).

With also observed significant correlations between HbA1c and cholesterol, triglycerides, HDL and LDL in diabetic patients. Several investigators have reported significant correlation between HbA1c and lipid profiles and suggested the importance of glycemic control and normalizing the dislipidemi. Although the levels of HbA1c did not differ between the two genders. The female patients showed significantly high levels of FBG (Table 2)

Diabetes confers a markedly increase risk of events in both males and females (Haffner SM., et colab 1998)

However, woman with diabetes are more susceptible to increased cardio vascular mortality. Diabetic woman may be subject to more adverse changes in coagulation, vascular function and cardiovascular risk factor than diabetic man (Walder C, et colab 1994 ; Hovard B, et colab 1998) The results of lipid profile showed that female diabetic patients had significantly higher levels of cholesterol and HDL, whitch is an agreement with early report. (Wexler DJ Grandt RW, et colab; Mohamad Met colab 1997). Hyperlipidemia in females may be attributed to the effects of sex hormones and body fat distribution, leading the differences in altered lipoproteins

High triglycerides and low HDL, but not hypercholesterolemia are the main features of dislipidemia observed in patients with metabolic syndrome (Bellomo A et colab 2007)

Recently, Avogaro et all (Avogaro A et colab) have suggested that type 2 diabetic dislipidemia in females and hyperglycemia in males are important risk factors are amenable to more aggressive treatment.

Results of univariate analysis have showed that HbA1c is a good predictor of triglyceride, followed by cholesterol, LDL and HDL .It has been reported that HDL cholesterol is inversely, and non HDL cholesterol directly, associated with CHD risk in diabetes patients (Eshaghian S et colab 2006)

Significantly high serum triglyceride levels have been found in diabetic patients with CHD as compared to non-diabetic patients (Esteghamaty A et colab 2006). Onat et al suggested that fasting triglycerides are predictive for future CVD independent of age, diabetes, total cholesterol in HDL.

The above discussion clearly indicated the clinical significance of various lipid parameters including total cholesterol, triglycerides, HDL and LDL in predisposing diabetic patients to cardiovascular complications

Significant correlations between HbA1c and all these lipid parameters, and a linear relationship between HbA1c and dislipidemia point towards the usefulness of HbA1c for screening high risk diabetic patients. Furthermore, there were o significant interaction between sex and age and HbA1c with respect to lipid profile, suggesting the validity of HbA1c for predicting dislipidemia irrespective of patient's gender and age

CONCLUSION

The levels of HbA1c did not differ significantly between males and females

HbA1c showed direct and significant correlations with cholesterol, tryglicerides and LDL cholesterol and reverse correlations with HDL cholesterol.

The findings of these study clearly suggest that HbA1c endures the ability of predicting serum lipid profile in both male ad female diabetic patients

Thus dual biomarker capacity of HbA1c (glycemic control as well as lipid profile indicator) may be utilized for screening high risk diabet patient for timely intervention with lipid lowering drugs.

There was no significant differences in tryglicerides and LDL cholesterol between the two genders

Both males and females patients with worse glycemic control (HbA1c > 9 %) had significantly high cholesterol and LDL levels.

These findings clearly suggest that HbA1c can provide valuable supplementary information about the extent of circulating besides its primary role in monitoring long term glycemic control

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