RELATIONSHIP BETWEEN HBA1C AND HYPERLIPIDAEMIA IN PATIENTS WITH DIABETES MELLITUS

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ABSTRACT:

Introduction: HbA1c is well now as predictor for hyperglycaemia due to accumulation of sugar on the Hb. The aim of this study is to now the relationship between HbA1c level and hyperlipidaemia. Patient and methods: this study was done in the diabetic and endocrine centre between 2010-2011 in which 187 patients involved, all of them had DM we send them for B.sugar,HbA1c, lipid profile including s.cholestrol, s.triglyceride, HDL, LDL and VLDL, renal function test. We divide them according to their sex, age, residency, work, family history of DM, past medical history of HT, atherosclerosis, IHD, smoking habit, type of drug used, albuminuria and type of DM. we use the chi square and exact test and SPSS 17 for statistics.

Results: 187 patients were involved in this study. 79(42%) were male and 108(58%) were female, there age was 3(1%) were less than 15 years, 74(40%) were in between 15-45 years and 110(59%) were more than 45years, HbA1c was divided into three groups the first one was less than 6 20(11%), 7-8 was 26(14%) and more than 8 was 141(75%). Strong relation ship between level of HbA1c and HDL (p=0.001), VLDL (p=0.027), s.cholestrol (p=0.004), s.triglyceride (p=0.05) and LDL (p=0.029).

Conclusion: strong correlation was found between HbA1c and all component of lipid profile in patients with DM, there fore HbA1c is a good predictor for hyperlipidaemia in DM

INTRODUCTION:

Glycohaemoglobin (HbA1c, A1c)

Glycohaemoglobin is a blood test that checks the amount of sugar (glucose) bound to hemoglobin. Normally, only a small percentage of hemoglobin in the blood (4% to 6%) has glucose bound to it. People who have diabetes or other conditions that increase their blood glucose levels have more glycohaemoglobin than normal(1). In a recent study by Selvin et al, (2) it was suggested that glycated hemoglobin values in the normal range can identify persons at increased risk for coronary heart disease, stroke, and death before the diagnosis of diabetes, indicating that glycated hemoglobin is a useful marker of cardiovascular risk and death from any cause. The glycohaemoglobin A1c is used to diagnose diabetes(1). The glycohaemoglobin A1c test checks the long-term control of blood glucose levels in people with diabetes(3). HbA1c may be separated by charge and size from the other hemoglobin A components in blood by a procedure called high pressure (or performance) liquid chromatography

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(HPLC)(4). The test does not change with any recent changes in diet, exercise, or medicines. Glucose binds to hemoglobin in red blood cells at a steady rate(5). Since red blood cells last 3 to 4 months, the glycohaemoglobin A1c test shows how much glucose is in the plasma part of blood. This test shows how well your diabetes has been controlled in the last 2 to 3 months(6) and whether your diabetes medicine needs to be changed. HbA1c may be increased falsely in certain medical conditions, these conditions include uremia (kidney failure), chronic excessive alcohol intake, and hypertriglyceridemia. Medical conditions that may falsely decrease HbA1c include acute or chronic blood loss, sickle cell disease or thalassemia(7). Diabetes during pregnancy, commonly referred to as gestational diabetes, may falsely increase or decrease HbA1c. Standardization for glycohaemoglobin from lab to lab varies, and you may not be able to compare a test from different labs unless you can verify the technique for measuring glycohaemoglobin is the same. The only exception is if your lab is standardized to the national DCCT referenced method(8). The American Diabetes Association and American Association of Clinical Endocrinologists recently endorsed the use of the HbA1c as a tool to diagnose diabetes, with a level of 6.5 or more indicating diabetes. This provides an alternative to the oral glucose tolerance or fasting glucose tests for the diagnosis of diabetes. Persons with an lesser degrees of HbA1c elevation (6.0 - 6.4) may still need a glucose tolerance test for the formal diagnosis of diabetes(9).

Cholesterol The body uses cholesterol to help build cells and produce hormones. Too much cholesterol in the blood can build up inside arteries, forming what is known as plaque. Large amounts of plaque increase the chances of having a heart attack or stroke.

HDL (high-density lipoprotein) helps remove fat from the body by binding with it in the bloodstream and carrying it back to the liver for disposal. It is sometimes called "good" cholesterol. A high level of HDL cholesterol may lower the chances of developing heart disease or stroke.

LDL (low-density lipoprotein) carries mostly fat and only a small amount of protein from the liver to other parts of the body. It is sometimes called "bad cholesterol." A high LDL cholesterol level may increase the chances of developing heart disease(10).

VLDL: (very low-density lipoprotein) contains very little protein. The main purpose of VLDL is to distribute the triglyceride produced by your liver. A high VLDL cholesterol level can cause the buildup of atherosclerosis in the arteries and increases the risk of heart disease and stroke.

Triglycerides are a type of fat the body uses to store energy and give energy to muscles. Only small amounts are found in the blood. Having a high triglyceride level along with high LDL cholesterol may increase the chances of having heart disease more than having only a high LDL cholesterol level(11,12&13).

Many studies demonstrate the relation ship between lipid profile and HbA1c where there is increase level of s. cholesterol, s.triglyceride, HDL, LDL VLDL with increase level of HbA1c.(14,15&16)

The aim of this study is to know the relationship between level of HbA1c and serum level of lipid profile.

PATIENTS & METHODS:

This study was performed in diabetes mellitus and endocrinology centre in Thi-

Qar in which 187 diabetic patients participate in this study we took full information and history including their age, sex, duration of diagnosis residency, their job, smoking, family history ,and past medical history including hypertension, history of IHD, CAD, arterial insufficiency, ..etc (atherosclerosis), and drug history ,body mass index was checked for all of them, then we send them to all the relevant investigations including RBS, FBS, lipid profile like HDL, VLDL, LDL, S.cholestrol and S.triglyceride and HbA1c,renal function test. Then to study the relation ship between HbA1c and lipid profile separately and whether HbA1c reflect the hyperlipidaemia state or not?. Fasting blood samples were obtained for blood sugar (venous blood samples taken after overnight fast of a minimum of 8 hrs) and; LDL was calculated using Friedwald formula. Measurements were made using minividas instrument (made in Italy), and the kit used was biomerieux (France) while the kit used for blood sugar was randox, s.cholestrol and s.triglyceride was bioLABO. The age was divided into three groups less than 15 years, 15-45 years and more than 45 years, many divisions was taken, according to time of occurrence of the complications and we divide them into two groups less than five years and more than five years, we exclude all patients with renal impairment. HbA1c is divided into three groups 6 or less which is sub diabetic level or very good control, 7 which is fair controlled DM and 8 or more which is poorly controlled and need action from the doctors. Then we study the relation ship between level of HbA1c and level of serum lipids.

RESULTS:

As shown in table (1), 187 diabetic patients 79(42%) patients male and 108(58%) were female. Their age range from 3(1%) patients less than 15 years , 74(40%)pt were in age between 15-45 years and 110(59%) patients were more than 45 years. 115(62%)pt they discovered to be diabetic in less than five years, the others more than five years. 114(61%)pt were in urban while 73(39%)pt from rural area. 104(55%)pt patients were house wives, 48(26%) patients were employed and 35(19%)pt were self worker. Regarding smoking 16(9%)pt were smokers and the others weren't. family history for DM were positive in 33(18%)pt and 154(82%)pt were negative . hypertension was positive in 46(25%)pt and were negative in 141(75%)pt. History of atherosclerosis as IHD, CAD, CVA, ..etc were found in 9(5%)pt only. The level of HbA1c = 6 or less is found in 20(11%)pt while those who had a level of 7-8 where 26(14%)pt and the last group with level more than 8 were 141(75%)pt. Then we check the body mass index for every patient and we divide them according to WHO classification. Another type of classifications was according to Type of drug used as a therapy as mentioned in the table. Then we studied the relationship between HbA1c and all types of lipid profile separately. Regarding HDL which is also called good cholestrol, as shown is table 2 there is increasing number of patients having low level of HDL with increasing level of HbA1c from 6(30%)pt in level 1 HbA1c to 95(67%)pt in level 3 HbA1c, and similarly decrease number of patients having high S.HDL from 70% in level 1 HbA1c to 33% in level 3 HbA1c; the dangerous level is less than 40mg\dl in male and less than 50 mg\dl in female, and it is clear the total number of patients with Low level of HDL was 117(63%) and 70(37%) for those with high level HDL (P=0.001). While VLDL, as shown in table 3 the cut point is

35mg\dl, the total number of patients with s.VLDL level is 85(45%) patients, with increasing number of patients having high level of VLDL from 4(20%) in level 1 to 66(47%) in level 3 and also decrease number of pt with low level of VLDL fro 80% in level 1 to 53% in level 3 with increasing level of HbA1c and this was statistically significant(P=0.027)indicate a good relationship between level of HbA1c and serum level of VLDL. That for s.cholestrol which was divided into three groups as shown in the table 4, we can see number of patients with high level s.cholestrol is 110 versus 77 with low level, and there is increase number of patients having high level of S.cholestrol with increasing level of HbA1c in all the three groups indicate a good relation ship between level of HbA1c and s.cholestrol level(P=0.004). About s. triglyceride the cut point between normal and abnormal level was 150mg\dl which is the minimal required level for the patient to enter criteria for metabolic syndrome, we can see also increase number of patients with high level of s.triglyceride with increase level of HbA1c, and there is a good relation ship between level of s.cholestrol in blood and HbA1c(P=0.05).as shown in table 5. Regarding level of LDL we can see increasing number of patients having high level of S.LDL with increasing level of HbA1c also and the number of patients with high level of LDL was 70 patients. And (P=0.029).

DISCUSSION:

In Betteridge DJ. Study the total cholesterol was normal to high in DM type 2(17), In another study the total cholesterol of 709 diabetic patients was significantly higher than that of control group (202.2 ± 41.5mg/dl vs. 189.0 ± 30.5 mg/dl, p<0.001), respectively(18).and many studies performed on Turkish population including 9,000 subjects between 1990 and 1993, total cholesterol level was found to be between 160 and 190 mg/dl. Total cholesterol levels of 68 per cent of the males and 78 per cent of the females were lower than 200 mg/dl. However, HDL levels of the population were reported to be lower than target levels. Therefore, an increased CAD risk was suggested due to the increased total cholesterol/HDL ratio(19). another study from Africa, consisting 401 type 2 diabetic patients, it was reported that 35% of patients had hypercholesterolemia(20), and a study from England showed that serum total cholesterol level was greater than 200 mg/dl in 73% of type 2 diabetic patients(21) In Murat study, 50% of diabetic patients had serum total cholesterol level of over 200 mg/dl(2).in our study agreat correlation has been found between s.cholestrol &HbA1c (P=0.004) as demonstrated increase level of HbA1c leads to increase number of patients having high s. cholestrol. Racial and nutritional factors have been suggested to explain these variations. Low level of HDL is well known risk factor for cardiovascular disease, A partial cause of low HDL in diabetic patients is the glycation of HDL and as a result an increase in HDL turnover(1). number of studies on HDL levels in type 2 diabetic patients reported that low HDL levels were common findings in comparison to non-diabetic control groups([22,23)] and another study by Onat and associates(24) showed that low HDL was a frequent finding among the population. In these studies, mean HDL levels of women were reported to be between 37 and 45 mg/dl, and in men, between 34 and 41 mg/dl and the HDL levels of 70% of men and 50% of women were reported to be below 40 mg/dl.in our

study a great correlation was found between HDL & HbA1c. (P=0.001)as we found when there is increase level of HbA1c there is high level of s.HDL as it is clear there is high risk of cardiovascular disease and deterioration in DM control. Hypertriglyceridemia is also a common finding in type 2 diabetic patients and Over production of VLDL and a decreased activity of serum lipoprotein lipase activity were suggested in the pathogenesis of Hypertriglyceridemia(24&25)a study by Reaven and associates(27), they showed a significantly positive correlation between serum insulin level and VLDL secretion. However, in several other studies, it was shown that acute hyperinsulinemia decreased VLDL synthesis in the liver of non-diabetics.(28&29).in our study the correlation was very clear between increasing level of HbA1c and s.triglyceride and VLDL, S.triglyceride &HbA1c (P=0.05) and VLDL &HbA1c (P=0.027) . Obesity and insulin resistance have been suggested to contribute to the pathogenesis of Hypertriglyceridemia in type 2 diabetics(28&29). Serum LDL cholesterol is the most atherogenic lipoprotein among serum lipoproteins. LDL cholesterol in type 2 diabetics is high or normal ranges. According to the criteria of NCEP ATP III, LDL cholesterol level over 100 mg/dl has been accepted as increased risk factor for CAD in diabetic patients.(30). in a similar study from India, LDL cholesterol level of 45.2% of type 2 diabetics was found to be higher than 130 mg/dl.(31). In a study from USA on LDL levels of type 2 diabetics, they reported that 58% of diabetic patients had serum LDL cholesterol over 130 mg/dl(32). this is similar to our study when there is good correlation between deterioration in level of blood sugar and LDL . Ethnicity, nutritional habitual and life styles could be a reason for the different LDL levels.

CONCLUSION:

1. HbA1c is a very good diagnostic test for diabetes mellitus that can give as an idia about the control of DM.
2. There is a clear relationship between HbA1c level and level of S.cholestrol, S.triglyceride, HDL, LDL, and VLDL.
3. most of the patients with uncontrolled DM and high HbA1c have a high level of s.cholestrol, triglyceride, LDL, VLDL and low level of HDL.
4. HbA1can be used as a predictor for hyperlipidaemia and hence as a risk factor for atherosclerosis and morbidity in patients with DM.
5. patients with high HbA1c need close observation than the other one due to high risk of complications than the other.

TABLES:

Table 1:- Characters of studied populations:-

Characters of patients	Number of pt	percentage
Sex male	79	42%
Female	108	58%
Age less than 15 y	3	1%
15-45 y	74	40%
More than 45 y	110	59%
Duration of disease		
Less than 5 y	115	62%
More than 5 y	72	38%
Residency		
Urban	114	61%
Rural	73	39%
Work		
House wife	104	55%
Employed	48	26%
Self work	35	19%
Smoking		
+ve	16	9%
-ve	171	91%
Family history		
+ve	33	18%
-ve	154	82%
Hypertension		
+ve	46	25%
-ve	141	75%
Atherosclerosis(IHD&CVA ….etc)		
+ve	9	5%
-ve	178	95%
HbA1c		
6-7	20	11%
7-8	26	14%
More than 8	141	75%
Body mass index		
Less than 20	4	2%
20-24.9	45	24%
25-29.9	64	34%
30-34.9	43	23%
More than 35	31	17%
Types of drug used		
Glibinclamide	82	44%
Metformin	17	9%
Glibinclamide&Metformin	54	29%
Insulin	28	15%
Diet only	6	3%

Table 2: - HDL & HbA1c(P=0.001)

		HbA1c=1	HbA1c=2	HbA1c=3	Total
HDL	1	6(30%)	16(62%)	95(67%)	117(63%)
	2	14(70%)	10(38%)	46(33%)	70(37%)
Total		20(100%)	26(100%)	141(100%)	187

1=male less than 40mg\dl, female less than 50mg\dl
2=male more than 40mg\dl, female more than 50 mg\dl

Table 3:- VLDL &HbA1c (P=0.027)

		HbA1c			
		1.00	2.00	3.00	Total
VLDL	1.00	4(20%)	15(58%)	66(47%)	85(45%)
	2.00	16(80%)	11(42%)	75(53%)	102(55%
Total		20(100%)	26(100%)	141(100%)	187

1= more than 35
2= less than 35

Table 4:- s.cholestrol &HbA1c (P=0.004)

		HbA1c			
		1.00	2.00	3.00	Total
S.cholestrol	1.00	2(10%)	5(20%)	33(23%)	40(22%)
	2.00	5(25%)	9(34%)	56(40%)	70(37%)
	3.00	13(65%)	12(46%)	52(37%)	77(41%)
Total		20(100%)	26(100%)	141(100%)	187

1= S.cholestrol >240mg\dl
2= S.cholestrol 180-240mg\dl
3= S.cholestrol <180mg\dl

Table5 :- S.triglyceride &HbA1c (P=0.05)

		HbA1c			
		1.00	2.00	3.00	Total
S.triglyceride	1.00	3(15%)	12(46%)	49(35%)	64(34%)
	2.00	17(85%)	14(54%)	92(65%)	123(66%)
Total		20(100%)	26(100%)	141(100%)	187

1=S.Triglyceride>200mg\dl
2=S.cholestrol <200mg\dl

Table 6:-S. LDL &HbA1c (P=0.029)

		HbA1c			Total
		1.00	2.00	3.00	
LDL	1.00	4(20%)	10(38%)	56(40%)	70(37%)
	2.00	16(80%)	16(62%)	85(60%)	117(63%)
Total		20(100%)	26(100%)	141(100%)	187

1=LDL>130mg\dl

2=LDL<130mg\dl

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بحث حول علاقة الهيموكلوبين المشبع بالكلوكوز في المرضى المصابين بداء السكر مع زيادة نسبة الدهون في الدم

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الخلاصة:

انه من المعلوم جيدا ان الهيموكلوبين المشبع بالسكريات هو دليل جيد على ارتفاع نسبة السكريات في الدم ، نحاول في البحث دراسة العلاقة بين زيادة نسبة الهيموكلوبين المشبع بالسكريات ونسبة الدهون في الدم.

المرضى والمواد المستخدمة: تمت الدراسة في مركز السكري والغدد الصماء في الفترة بين ٢٠١٠ ـ ٢٠١١ حيت انضم حوالي ١٨٧ مريض كلهم مصاب بداء السكري أرسل جميع المرضى لمجموعة من التحاليل المختبرية من ضمنها نسبة السكر مع الهيموكلوبين .نسبة الدهون،وظائف الكليتين تم تقسيم المرضى طبقا الى الجنس، العمر، تاريخ المرض، تاريخ العائلة السكن،الوظيفة، نسبة الألبومين في الدم مع نوع السكر ونوع العلاج المستخدم.

النتائج:

١٨٧ مريض تم دراستهم. ٧٩ (٤٢%) كانوا من الذكور و ١٠٨ (٥٨%) كانوا من النساء. كانت أعمارهم تتراوح بين ٣(١%) في الأعمار تحت ١٥ سنة الى ٧٤ (٤٠%) للمرضى بين ١٥ ـ ٤٥ سنة و ١١٠ (٥٩%) للمرضى الأكثر من ٤٥ سنة، وكان عدد المرضى الحاملين الهيموكلوبين المشبع بالسكر وحسب مستوى الهيموكلوبين ٢٠(١١%) لتركيز اقل من ٦، ٢٦(١٤%) لتركيز ٧ – ٨ بينما ١٤١(٧٥%) مريض لتركيز أكثر من ٨ .العلاقة بين مستوى الهيموكلوبين ونسبة الدهون في الدم كانت كالتالي مع نسبة الاحتمالية الإحصائية الدهون بمستوى الكثافة العالية (نسبة الاحتمالية تساوي ٠,٠٠١) الدهون الخفيفة جدا بالكثافة (٠,٠٢٧)و الكولسترول في الدم (٠,٠٠٤) ، الدهون الثلاثية تساوي (٠,٠٥) والدهون ذات الكثافة الواطئة (٠,٠٢٩).

الاستنتاج:

توجد علاقة وطيدة وقويه بين مستوى الهيموكلوبين في الدم المشبع بالسكر وبين مستوى الدهون في المرضى المصابين بالسكري.

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