Correlation between ABO blood group and Dyslipidemia with Metformin therapy in newly diagnostic type 2 Diabetes Mellitus

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Abstract : Type 2 Diabetes mellitus is a globally growing chronic disease. Metformin the first line therapy for newly diagnosed type 2 diabetes mellitus. The etiology of type 2 diabetes including obesity, environmental effect, genetic susceptible, blood groups consider one of genetic susceptible. The aim of present study to investigate relationship between ABO blood group and dyslipidemia with metformin effect as first line treatment in type 2 diabetes mellitus newly diagnosed. Fifty five patients newly diagnosed type 2 diabetes mellitus collected in diabetic center Al- Husseini hospital by specialist physician according American Association Diabetes, from December 2015 to May 2016.Blood group A had more reduction in Total cholesterol (TC), and low density lipoprotein (LDL) compared with other blood groups. While B blood group offer only more significant reduction in Triglyceride (TG) compared the other blood groups. Patients with blood group A show improved response to metformin therapy by reduction of TC and LDL which was better than the improvement in lipid profile offer by other blood group (B, AB). Patients with blood group O show no significant effect on lipid profile with using metformin therapy.

Introduction

Diabetes is a metabolic condition in which the body does not produce sufficient insulin to regulate blood glucose levels or where the insulin produced is unable to work effectively, diabetic classified into 2 types, (1) diabetesI is an auto-immune condition in which the cells that produce insulin in the pancreas are destroyed which resulted in lifelong treatment with insulin is mandatory; about 10% of people with diagnosed diabetes have type 1 diabetes, (2) the second type II diabetes accounts for at least 90% of all cases of diabetes,it occurs when the body either stops producing enough insulin for its needs or becomes resistant to the effect of insulin

produced. The etiology of diabetes mellitus (DM) is complex and multifactorial, and factors such as immunological, genetic and environmental are involved[1].

Obesity has a complex relationship with diabetic and diabetes mellitus is strongly associated with obesity[2].It is stands out as a risk factor for Type 2 DM;in which it may be a precursor for Type 2 DM, following insulin resistance[3]. Most researchers consider that this relationship is different in different types of obesity and Type 2 DM[4].Many studies demonstrated the role of ABO blood groups in type2 DM, the A allele (blood types A or AB) were less likely to have type 2 DM than those of type B or O and Rh positive was associated with type2DM[5].While blood group B was associated with type2 DM in another report[6].Numerous studies have been completed to establish a relative between blood group and obesity, it is not clear if that role is large or small, associated to lifestyle or genetics [7].

The correlation of ABO groups with perceived stress and its effect on lipid profile appeared to be strong,in study conducted to find the association of apparent stress with blood group A and O between and its end product on lipid profile in a medical college of eastern India, people with blood group O are more susceptible to duodenal ulcers and perceived stress. Therefore subjects with blood group O had more stress as compared to subjects of blood group A and perceived stress significantly worsened LDL‑C levels. [8].

The cholesterol level is an indicator for the associations of ABO group with CAD and MI.A number epidemiological studies have shown that person of a non-O type (A, B, or AB type) are most likely to have CHD than O type person[9].Recently have been exposed in genetic studies of the variation at the ABO locus and relationship of ABO group with total cholesterol (TC) and LDL-c level[10]

Treatment of DM type 2 must include pharmacological agents able to improve not only glycemic levels, but also blood pressure (BP), lipid levels, and body weight, since in approximately 90% of type 2 diabetics hyperglycemia is associated with other cardiovascular factors that constitute the metabolic syndrome. Metformin lifestyle intervention should be starting at the stage of diagnosis Type2 diabetes; it's effective and safe as initial management hyperglycemia[11]. Metformin increased free fatty acid esterification clearly and inhibition of lipolysis in adipose tissue.[12].Several studies were undertaken to assess its effects on total cholesterol (TC), triglycerides (TG), and HDL-cholesterol (HDL-C) levels[13].

The objective of this study was to investigate the relationship between ABO blood groups and dyslipidemia with (metformin) effect as first line in treatment of Type 2 diabetes in newly diagnosed.

Subjects and Methods

Study design and Subjects

This study was prospective clinical trial carried out at the Specialist Al Hussein Center for Diabetes and Endocrinology in Iraq. Fifty five of newly diagnosis type 2 diabetes mellitus by specialist physician in diabetic. The study participants were patients with type 2 diabetes (35 men and 20 women). All patients must take metformin treatment (1500mg) signal dose for three months. Written agreement for participation taken from each patient, and this study follow Helsinki declaration for protection of participants in the study.

Samples Collection then Preparation

After 12 hours fasting, blood sample was collected for all patients and control, one milliliter of blood was tested closely following collected directly. Anti-A, anti-B and anti-D monoclonal blood group reagents were always used to define the ABO and Rh (D) phenotype by slide method agglutination at room temperature. Another blood samples were mainly collected in Gel tube and centrifuged by 3000 rpm for 5 minutes to get serum for measuring of (TG,Serum cholesterol, LDL,and HDL).

Statistical analysis

Continuous data was tested using Anderson Darling test to clarify if they follow normal distribution. Continuous data that follow normal distribution presented using there mean and standard deviation, those that did not normal distribution presented using there median and interquartile range (IQR; 25% to 75% of the data). Paired t test and independent t test (between patients and control) was used (for normally distributed data).

Mann Whitney U test to analyze the difference in median between 2 groups (non- normally distributed data), if 2 paired groups Wilcoxon rank test used.

Results

Fifty five patients with newly diagnostic Type 2 diabetes were included in this study. Diabetes patients assigned into four groups, according on blood group (AB, B, A, and O).All four groups receive metformin for 3 months. In addition thirty two subjects reference were included as healthy control group, table 1 illustrate the demographic data of the patients and control.

Table 1: **Demographic Data and Baseline Characteristic of the Patients**				
		Control	Patients	P value
Number		32	55	-
Age (years)		46.1 ± 9.7	46.9 ± 9.7	0.713 [NS]
BMI (kg/m^2)		25.3 ± 1.3	32.5 ± 4.6	<0.001 [Sig.]
Gender				0.852 [NS]
	Female	11 (34.4%)	20 (36.4%)	
	Male	21 (65.6%)	35 (63.6%)	
NS: non-significant, Sig.: significant difference				
Independent t test, chi square test				

Blood groups (A, B and AB) had significantly reduced total cholesterol in 3 months duration of therapy, while blood group O subjects did show significant reduction in total cholesterol as illustrated in table 2.Only blood group B had significant reduction in triglyceride, while the rest of blood groups had non-significant reduction as illustrated in table 3. Table illustrated the effect on HDL in which all blood groups did not show significant change over 3 months of metformin therapy. Only patients with blood group A show significant reduction in LDL, while the rest of the blood groups show no significant change in LDL as illustrated in table 4.
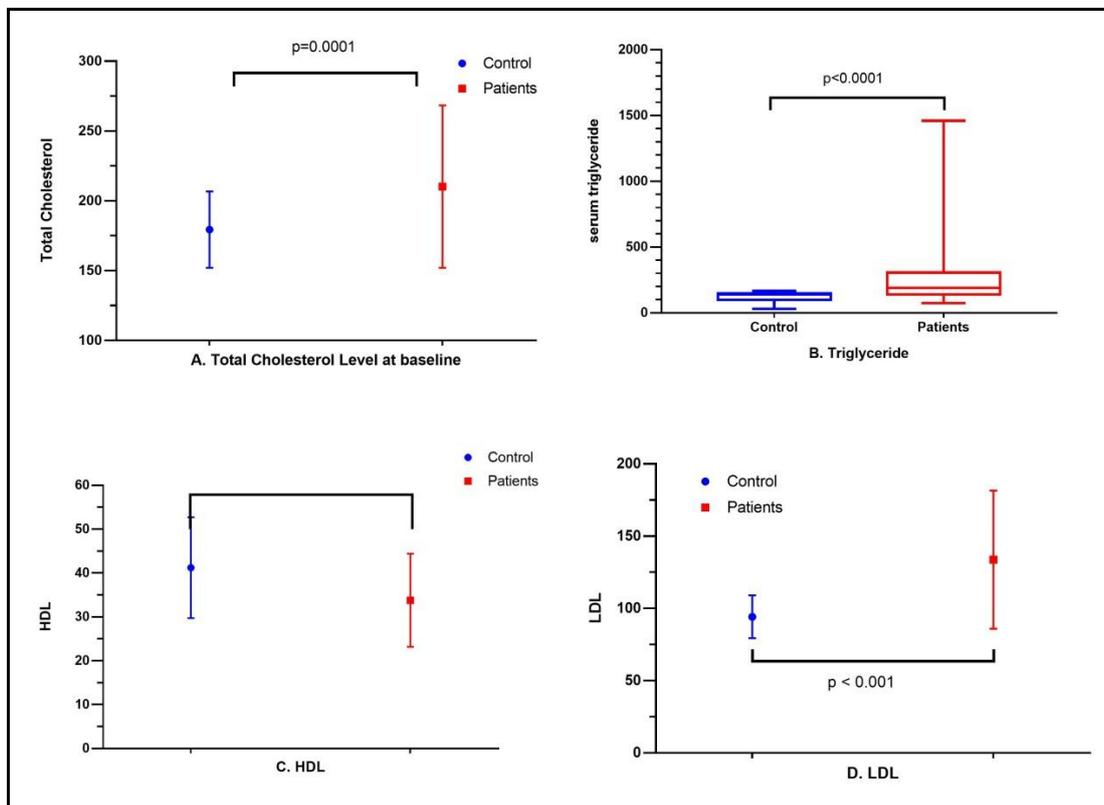

Figure 1: comparison between lipid profiles of all patients versus control at baseline

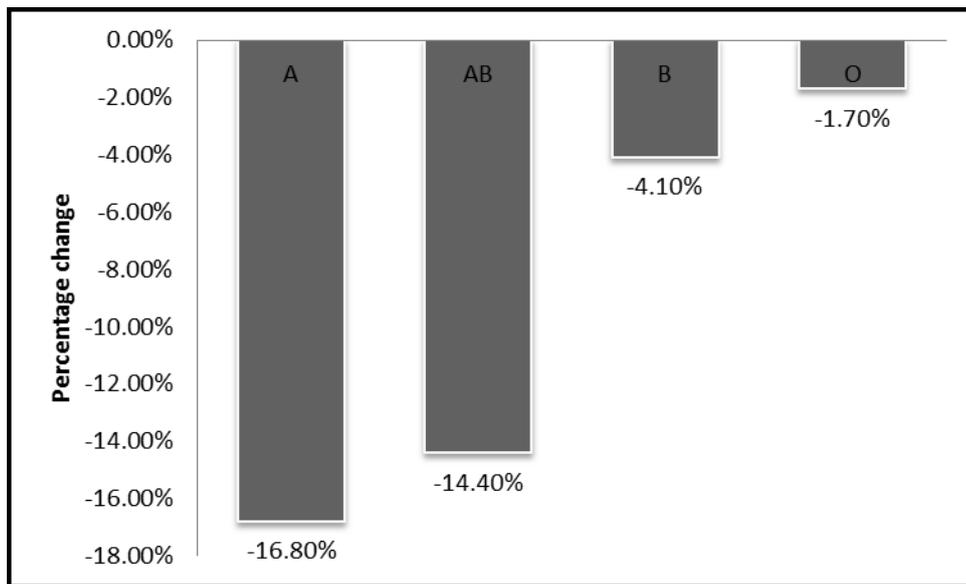| Table 2: Effect of metformin on Total Cholesterol Level in new detected patients with Type 2 DM at different blood groups after 3 months			
	Patients (baseline)	**Patients (after 3 months)**	**P value**
All (n=55)	210.2 ± 58.2	189.0 ± 39.3	0.004 [Sig.]
Blood groups			
A (16)	242.9 ± 52.4	202.1 ± 38.4	0.007[a] [Sig.]
AB (12)	210.4 ± 72.4	180.1 ± 37.2	0.028[b] [Sig.]
B (14)	190.1 ± 46.8	182.4 ± 41.5	0.048[b] [Sig.]
O (13)	191.5 ± 48.6	188.3 ± 40.0	0.832[a] [NS]
NS: non-significant, Sig.: significant difference			
[a] **Paired t test,** [b] **Wilcoxon rank test**			

Figure 2: showing percentage reduction in total cholesterol for each blood group.

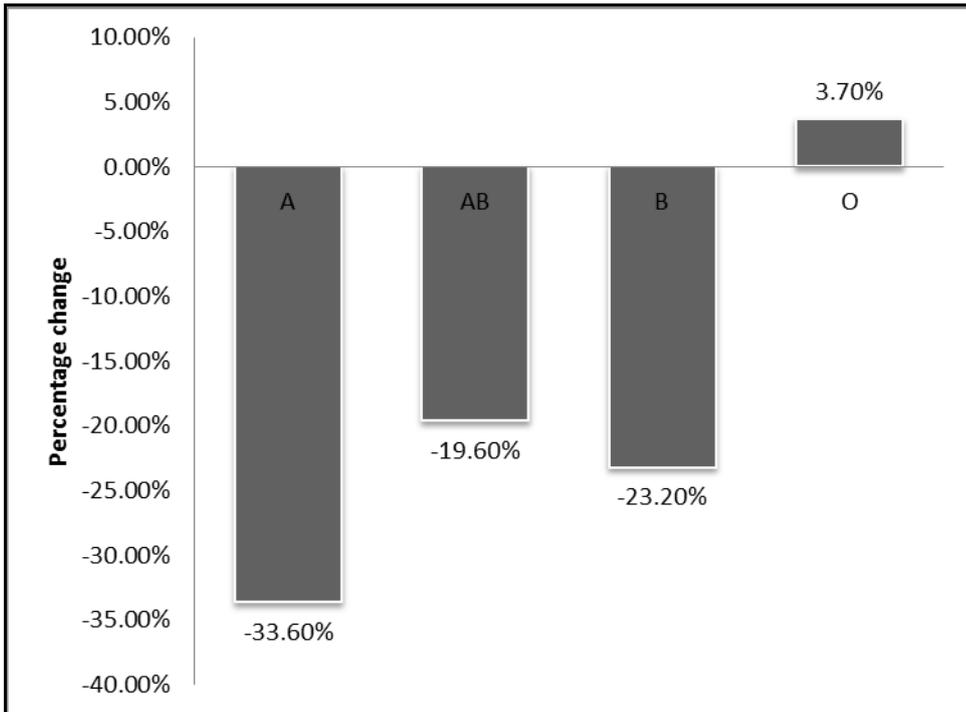| Table 2: Effect of metformin therapy on Triglyceride in new detected patients with Type 2 DM at different blood group after 3 months			
	Patients (baseline)	**Patients (after 3 months)**	**P value**
All (n=55)	189 (140 – 306)	165 (113 – 248)	0.004 [Sig.]
Blood groups			
A (16)	250 (161 – 347)	166 (118 – 446)	0.156 [NS]
AB (12)	168 (117 – 274)	135 (95 – 236)	0.583 [NS]
B (14)	185 (135 – 273)	142 (101 – 192)	0.030 [Sig]
O (13)	187 (146 – 292)	194 (109 – 259)	0.108 [NS]
NS: non-significant, Sig.: significant difference			
Wilcoxon rank test			

Figure 3:showing percentage reduction in triglyceride for each blood group.

Table 3: Effect of metformin therapy on HDL in new detected patients with Type 2 DM at different blood group after 3 months			
	Patients (baseline)	Patients (after 3 months)	P value
All (n=55)	33.8 ± 10.6	36.3 ± 8.6	0.074 [NS]
Blood groups			
A (16)	34.8 ± 7.7	34.8 ± 7.5	0.987 [NS]
AB (12)	33.1 ± 10.7	36.9 ± 9.1	0.355 [NS]
B (14)	33.2 ± 9.7	37.5 ± 8.4	0.082 [NS]
O (13)	33.7 ± 15.0	36.4 ± 10.4	0.449 [NS]
NS: non-significant, Sig.: significant difference Paired t test			

Figure 4:showing percentage reduction in HDL for each blood group.

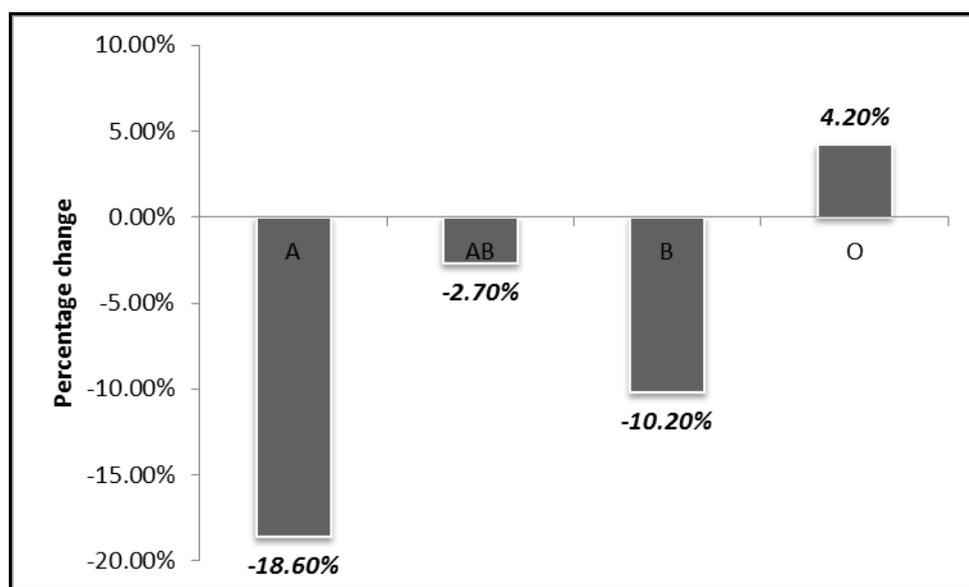| Table 4: Effect of Table 4: Effect of metformin therapy on LDL in new detected patients with Type 2 DM at different blood group after 3 months			
	Patients (baseline)	Patients (after 3 months)	P value
All (n=55)	133.7 ± 47.8	122.5 ± 34.6	0.043 [Sig]
Blood groups			
A (16)	153.0 ± 57.7	124.6 ± 40.5	0.027 [Sig]
AB (12)	121.9 ± 26.3	118.6 ± 31.1	0.465 [NS]
B (14)	132.2 ± 56.7	118.7 ± 34.0	0.166 [NS]
O (13)	122.4 ± 35.1	127.6 ± 33.8	0.703 [NS]
NS: non-significant, Sig.: significant difference Paired t test			

Figure 5:showing percentage reduction in LDL for each blood group.

Discussion

The results of present study are compatible with previous studies in which met form in reduced total cholesterol (TC),triglyceride(TG),low density lipoprotein(LDL-c) level significantly, and increase but non-significantly in high density lipoprotein cholesterol(HDL-c)level compared with baseline values. In addition, the results in present study support using of metformin for improve lipid profile in diabetes patients[14].

In another study that observed different blood groups (A,AB, and B) these blood groups showed similar effect on total cholesterol,whereas blood group O had lower effect in compared to other[15].This may suggest that (A,AB, and B) blood groups more response to metformin therapy on total cholesterol in blood. This observation is similar to our finding on total cholesterol.

In our study only B blood group had significantly decreased TG level in compared to baseline values, while the other groups had none significant effect. Jingazhou Wang observed that (A, AB, and O) blood groups significantly higher in level with triglyceride in blood, while B blood group did not change TG and had less chance for having (CVD)[16].This may suggest that B blood group more response to metformin treatment on triglyceride in blood. All blood groups in our study had non-significant increase in HDL-c compared baseline. Only A blood group had significant decrease in LDL-c compared with baseline (after 3 months),while, the other groups had non-significant change. Chaudhuri et al found that A blood group had higher level LDL-c compared with O blood group [17].This may suggest A blood group is more response to metformin treatment. Yasunori observed elevated LDL-c, total cholesterol and triglyceride level with increased E-select in concentration and decreased by reduction in LDL-c, total cholesterol, triglyceride level[18],also metformin decreased E-selectin

concentration[19],which suggest ABO blood groups association with E-selectin concentration , lead to various response to metformin treatment.

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