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Research Article

ABO BLOOD GROUPS IN CORRELATION WITH HYPERLIPIDEMIA, DIABETES MELLITUS TYPE II, AND ESSENTIAL HYPERTENSION

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ABSTRACT

Objectives: There are associations between ABO blood groups and systemic diseases. So we aim to explore any associations among ABO blood group with hyperlipidemia; diabetes mellitus (DM) type II, and essential hypertension.

Methods: A total of 800 subjects were recruited. Patients groups were subdivided into hyperlipidemia group (n=100), DM type II group (n=160), and hypertension group (n=166). Fasting blood sample was collected and plasma samples used for measuring of 2, 3-dinor-6-keto-prostaglandin-$F_{1\alpha}$ (PGF1α), 11-dehydro-thromboxane (TX) B_2, insulin, triglycerides (TGs), total cholesterol (Tc), high-density lipoprotein cholesterol (HDL-C), prothrombin time (PT), activated partial PT (aPPT), blood group type, random blood glucose level, and body mass index (BMI) were also determined.

Results: Blood Group A demonstrates a significant elevation in insulin, random blood sugar (RBS), Tc, TGs, and low-density lipoprotein (LDL)/HDL ratio and shows a significant decrease in prostacyclin. Blood group B demonstrates a significant elevation in TXB_2, Tc, TGs, and LDL/HDL ratio and shows a significant decrease in PT. Blood group AB demonstrates a significant elevation in PT, and prostacyclin and shows a significant decrease in insulin, RBS, Tc, TGs, and LDL/HDL. Blood group O demonstrates a significant elevation in PT, and prostacyclin and shows a significant decrease in TXB2, Tc, TGs, and LDL/HDL ratio.

Conclusions: Blood group AB is protective against hyperlipidemia, diabetes, thrombosis, and hypertension, blood group O is protective against cardiovascular diseases while blood group B followed by A are risk factors for hypertension and blood group A is a risk factor for diabetes. These findings are establishing the ethnic-dependent correlation of ABO groups and studied diseases.

Keywords: Hyperlipidemia, DM type II, Hypertension, Thrombosis, ABO blood groups.

INTRODUCTION

The ABO system occurs as a result of polymorphism of complex carbohydrate with different antigenic structures of glycoproteins and glycolipids expressed at the surface of erythrocytes, as glycan units of mucin glycoproteins [1,2].

The A and B alleles of the ABO, locus encode A and B glycosyltransferase activities, which convert precursor H antigen into either A or B determinants, the A and B antigens having an extra saccharide unit to the O unit (N-acetylgalactosamine and galactose, respectively). Group O individuals lack such transferase enzymes (loss of function) and express basic, unchanged H-antigen [1].

The clinical significance of ABO blood type is not only limited to blood transfusion and solid organ or hematopoietic transplantation but also its correlation to various systemic diseases has been investigated. Various reports have suggested important associations between ABO blood groups and systemic diseases, such as, gastric cancer and peptic ulcers, cholera, pancreatic cancer, type II diabetes mellitus (DM), thrombotic vascular diseases [3], maxillofacial deformities [4], and placental malaria infections [5].

Gender, age, obesity, smoking, body mass index (BMI), DM, hypertension, and family history are considered major cardiovascular and atherosclerosis risk factors. Several studies have revealed that ABO blood groups, particularly non-O blood groups, are associated with major cardiovascular risk factors and/or increased rate of cardiovascular events [6-9].

A clear correlation has been established between ABO phenotype and the level of two proteins involved in blood clotting, von Willebrand factor (vWF), and factor VIII [10].

DM is a multi-factorial trait. The etiology of DM is complex and appears to involve inter-actions of genetic, immunological, and environmental [11]. However, there is evidence regarding the role of blood group in DM type II [12].

Although several studies have been carried out to investigate the association between ABO blood group and incidence of many systemic diseases, but the reasons for such associations are remain controversial, several investigations have been made to explore the relationships between ABO blood groups and markers of some diseases.

This study aimed to explore any possible associations between ABO blood group with hyperlipidemia, DM type II and essential hypertension among Yemeni Subjects using hematological and biochemical tools. The novelty of this work is to study whether the previously published data is a universal correlation, or it is an ethnic-dependent correlation.

METHODS

Disease criteria

Essential hypertension described according to The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (BP) criteria [13]. Any individual with raised BP values of systolic BP above 140 mm of Hg and diastolic BP above 90 mm of Hg was classified as hypertensive and pulse rate was recorded from the beats of the radial artery. Systolic and diastolic BP of each subject was taken using manual mercury sphygmomanometer and stethoscope, BP measurements were done by physicians while patients in a resting state at least for 15-20 minutes. DM type II diagnosed according to the American Diabetes Association [14]. Hyperlipidemia defined according to the National Cholesterol Education Program of the National Heart Blood and Lung Institute [15].

Inclusion criteria
In the current study, during March, 2013 to February, 2014 a total of 800 subjects were recruited comprised of 426 patients groups from hospital out-clinic and 374 control groups. The patients groups were subdivided to hyperlipidemia group (100 patients), DM type II group (160 patients), and hypertension group (166 patients). All subjects in each group have a family history of the same disease only. Control groups were 200 healthy subjects for DM type II and hyperlipidemia then a second group comprised of 174 healthy subjects for hypertension (all control groups are devoid from any studied diseases and this were confirmed by required blood tests). The unrelated normal healthy individuals were sampled randomly from the same area matching age, sex, and socio-economic status.

All recruited subjects' data such as age, education, occupation, number of children, smoking, alcohol, khat chewing, and any current disease or medication were collected using a detailed questionnaire as a routine patient history record file in the Al-Kuwait Hospital in Sana'a of Yemen Republic.

Exclusion criteria
The subjects with a history of tobacco smoking, alcohol, Khat chewing, addiction history, and any chronic disease other than those considered in the current study were excluded. Subjects administering any of the following drugs; steroids, oral contraceptives, diuretics, and beta blockers were also excluded from the study.

Materials and equipment
Thromboxane (TX) A_2-stable metabolite (11-dehydro-TX B_2); prostacyclin (PGI_2)-stable metabolite (2,3-dinor-6-keto prostaglandin F1α (PGF1α)); ultra-pure water free of organic contaminant traces and deionized is used to prepare all ELISA reagents and buffers (ultra-pure) using kits from Cayman (Cat. No. = 519510), (Cat. No. = 515121), and (Cat. No. = 400000), respectively. Insulin is measured by Mercodia Insulin ELISA kits for serum and plasma, 8A, SE-754 50 Uppsala, Sweden. ELISA measurements were performed by plate ELISA reader (Humareader Human Company 2106/1682) capable of measuring absorbance at 405-420 nm. Total cholesterol (Tc), triglycerides (TGs), and high-density lipoprotein cholesterol (HDL-C) were measured using colorimetric methods on spectrophotometer (Shimadzu).

Prothrombin time (PT), and activated partial PT (aPPT) were measured by Coagulometer (Biomatic Biosarstedt, Freiburg, Germany) and UV/visible spectrophotometer (Shimadzu). ABO blood types, standard serological procedures were followed using the anti-A, anti-B, and anti-D antisera by standard agglutination techniques. BMI was calculated according to equation;

Body mass index (BMI) = weight (kg)/length^2 (m^2).

Blood sample collection, hematological, and biochemical methods
Fasting blood sample (9 ml) was collected from each subject and the first 6 ml aliquot of blood was taken on sodium heparinized vials for plasma separation (Centrifuge, Hitachi, Germany) and refrigerated at −20°C until used for measuring prostacyclin (PGI_2)-stable metabolite (2,3-dinor-6-keto-PGF1α), 11-dehydro-TX B2 (a stable metabolite of TXA_2), and insulin with ELISA kits.

TGs were estimated using the phosphate oxidase method as described by Trinder [16], Tc was estimated using the Chod–Pap method as described by Zoppi and Fellini [17], HDL-C was estimated using the dextran–sulfate Mg(II) method as described by Wieland and Siedel [18], and low-density lipoprotein cholesterol (LDL-C) calculated using Friedewald *et al*. [19] formula;

LDL = Tc − HDL − TG/5.0 (mg/dL)

The second 3 ml aliquots of blood samples were taken into citrated blood sampling vials and separated plasma immediately after collection, PT, and aPPT were measured as described by Dacie and Lewis [20] using an automated coagulometer (Biomatic Biosarstedt, Freiburg, Germany).

Random blood glucose (RBG) level was measured by glucose kit (Glucose-GOD-POD, SPINREACT, S.A./S.A.U Ctra.Santa Coloma, and 7 E-17176 SANT ESTEVE DE BAS (GI) SPAIN). Height (cm) and weight (kg) were measured by anthropometer and weighing instrument, respectively. BMI, which is the most common used indicator of obesity in population studies, was determined by calculation, weight in kilograms divided by height in meters squared (kg/m^2) [21].

All the above studied (hematological and biochemical) parameters were measured at the central laboratory of Al-Kuwait hospital.

Ethical consideration
The current study was carried out as a case-control study. The research protocol is following all the ethical regulations stated by the ethical committee in the university and being approved. Written consent was taken from all participants as a routine hospital protocol, as the Al-Kuwait Hospital Sana'a, Yemen is a charge-free governmental hospital, and all patients were informed that their diagnosis and biological samples taking during diagnosis could be used anonymously for education and research purposes. All our blood samples were collected during regular and routine diagnosis procedure for patients without using any invasive protocols.

Data analysis
Data were collected and analyzed using SPSS version 15 (SPSS Inc, Chicago, IL). Two ways ANOVA (multivariate comparison) Pillai's Trace, Wilks' Lambda, Hotelling's Trace, and Roy's largest root were used to assess the difference between means and frequencies (the associations between tested parameters, Blood ABO groups, and subjects clinical status). *Post-hoc* analysis was used to test the difference between subgroups means and subsets homogeneity. Observed difference was considered to be significant at $p<0.05$.

RESULTS

Table 1a shows the number of the patients, controls and their sex percentage in all recruited subjects for each disease and blood group. Hyperlipidemia is demonstrated in Blood group A (37%), group B (33%), group AB (12%), and group O (18%) where group A is the highest and group AB is the lowest. DM is demonstrated in blood group A (37.5%), group B (31.25%), group AB (12.5%), and group O (18.75%) where group A is the highest and group AB is the lowest. Hypertension is demonstrated in Blood group A (30%), group B (48.5%), group AB (13.8%), and group O (7.2%) where group B is the highest and group O is the lowest.

Table 1b shows the significant effect of each blood group and sex within this group on the clinical status of patients and control groups. Sex shows the insignificant effect in all investigated diseases while ABO groups were highly significant in all diseases.

Pair-wise comparison between males and females to determine the sex effect on TXB2, aPPT, 2,3-dinor-6-keto-PGF1α and PT showing the total insignificant effect of sex on all tested markers at $p<0.05$.

Tables 2-4 show the mean values of all investigated markers related to hyperlipidemia, diabetes and hypertension in recruited subjects at $p<0.05$ between patients and control groups for each ABO blood group type in each disease group. Significance was tested for total subjects within a specific blood group and disease in relation to total subjects in the corresponding control group excluding sex and BMI which showed insignificant effect.

In Tables 2-4, blood group A demonstrates a significant elevation in insulin, RBG, Tc, TGs, and LDL/HDL ratio and shows a significant decrease in 2,3-dinor-6-keto-PGF1α and had no effect on TXB_2 and PT.

Table 1a: Distribution of ABO blood group in patients with hyperlipidemia, diabetes mellitus, essential hypertensive patients, and healthy controls (total subjects = 800)

Variable	Patients (n=260) [N (%)]		Controls (n=200) N (%)	Patients (n=166) [N (%)]	Controls (n=174) N (%)
	Hyperlipidemia (n=100)	Diabetes mellitus type II (n=160)		Essential Hypertension (n=166)	
Blood groups					
A	37 (37)	60 (37.5)	65 (32.5)	50 (30.1)	65 (37.3)
B	33 (33)	50 (31.25)	75 (37.5)	81 (48.7)	49 (28.1)
AB	12 (12)	20 (12.5)	20 (10)	23 (13.8)	20 (11.4)
O	18 (18)	30 (18.75)	40 (20)	12 (7.2)	40 (22.9)
Sex					
Male	45 (45)	70 (43.75)	120 (60)	119 (71.6)	105 (60.3%)
Female	55 (55)	90 (56.25)	80 (40)	47 (28.3)	69 (39.6%)

Table 1b: Multivariate tests for all parameters in each disease testing the effect of blood group and sex on clinical status

Effect	Test											
	Pillai's trace			Wilks' lambda			Hotelling's trace			Roy's largest root		
	Value	F	Significant	Value	F	Significant	Value	F	Significant	Value	F	Significant
Insulin, RBS and BMI in diabetic patients and control groups												
Clinical status * Blood group	0.209	8.596	0.000	0.795	9.155	0.000	0.253	9.583	0.000	0.231	26.535	0.000
Clinical status * Sex	0.005	0.621	0.602	0.995	0.621	0.602	0.005	0.621	0.602	0.005	0.621	0.602
Prothrombin Time, aPPT, prostacyclin and TXB2 in hypertensive patients and control groups												
Clinical status * Blood group	0.688	24.042	0.000	0.410	28.348	0.000	1.200	31.972	0.000	0.959	77.406	0.000
Clinical status * Sex	0.009	0.701	0.592	0.991	0.701	0.592	0.009	0.701	0.592	0.009	0.701	0.592
T. Cholesterol, TGs, LDL, HDL and LDL/HDL ratio in hyperlipidemia patients and control groups												
Clinical status * Blood group	0.860	22.676	0.000	0.268	31.463	0.000	2.247	41.738	0.000	2.009	113.326	0.000
Clinical status * Sex	0.037	2.149	0.060	0.963	2.149	0.060	0.038	2.149	0.060	0.038	2.149	0.060

$p<0.05$. Clinical status (healthy controls/patients); blood group (A, B, AB, O); sex (male/female)

Blood group B demonstrates a significant elevation in TXB_2, Tc, TGs, and LDL/HDL ratio and shows a significant decrease in PT and shows no effect on insulin, random blood sugar (RBS), and prostacyclin. Blood group AB demonstrates a significant elevation in PT and prostacyclin ratio and shows a significant decrease in insulin, RBS, Tc, TG, and LDL/HDL and shows no effect on TXB_2.

Blood group O demonstrates a significant elevation in PT and 2,3-dinor-6-keto-PGF1α and shows a significant decrease in TXB2, Tc, TGs, and LDL/HDL ratio and shows no effect on insulin and RBG.

Tables 5a and b illustrate the ABO group's effect on all studied parameters and its correlation with all studied diseases, respectively. Combination effect for several markers together shows group O is the only group significantly affects PT, 2,3-dinor-6-keto-PGF1α, and TXB_2 while groups A and AB significantly affect insulin and RBS then all blood groups significantly affect Tc, TGs, and LDL/HDL ratio.

DISCUSSION

The high prevalence of a particular blood group in a community or geographical area may affect the incidence of diseases [22].

ABO blood groups and Hyperlipidemia

Cardiovascular disease such as coronary artery disease (CAD) is one of the leading causes of morbidity and mortality worldwide and is proportional to the levels of serum cholesterol, LDLc, and very LDL [23]. A possible genetic interaction between ABO blood groups and CAD is reported, because the gene involved in the cholesterol balance ATP-binding cassette 2 (ABCA2) and ABO blood groups are located on chromosome 9 (locus 9p34) [24] and ABO blood group might influence plasma lipid levels [25].

Genome-wide association studies (GWASs) and their meta-analyses support the role of ABO genotypes in modulating circulating levels of LDL and Tc establishing causal risk factors for atherosclerotic heart diseases. Additional meta-analysis of 46 lipid based GWAS reported an association between ABO single nucleotide polymorphisms (SNPs) and serum cholesterol levels [26].

The current study illustrated high Tc, TGs, LDLc, and lower HDLc in blood groups A & B while groups O and finally AB showed low levels of Tc, TGs, and LDLc which comes in agreement with reports from [25, 27] stating that blood group A showed the higher levels of serum Tc and LDL-C in Japanese and in white adults and adolescents cohorts while Stakisaitis *et al*. [28] and Napoli *et al*. [29], were in agreement for group A and were in contrary for groups AB and O in British men as they followed group A in hyperlipidemia.

ABO blood groups and essential hypertension

ABO system and hypertension

Hypertension is a worldwide problem with serious implications in terms of increased morbidity and mortality rates.

The current study illustrated blood group B followed by blood group A had the highest risk factor for hypertension and this data come in agreement with Sachdev [21] who observed that those carrying

Table 2: Mean levels of Tc, TGs, LDL, HDL, and LDL/HDL ratio in hyperlipidemia patients and healthy controls versus ABO blood group

Clinical status * blood group * sex	Mean±SD				
	Tc (mg/dL)	TGs (mg/dL)	LDL (mg/dL)	HDL (mg/dL)	LDL/HDL ratio
Patients (n=100)					
A (37 [37%])					
Sex					
Male (n=13)	290.61±12.25	280.61±10.82	196.10±9.74	38.38±3.68	5.15±0.64
Female (n=24)	305.16±10.05	296.33±10.31	207.90±8.31	37.95±2.49	5.53±0.44
Total=37	300.05±12.81$^{\&}$	290.81±12.84$^{\&}$	203.75±10.40$^{\&}$	38.10±2.92$^{\&}$	5.39±0.54$^{\&}$
B (33 [33%])					
Sex					
Male (n=26)	288.30±4.56	279.80±5.55	197.11±5.17	35.23±2.10	5.61±0.40
Female (n=7)	294.71±4.11	282.28±4.75	203.54±4.79	34.71±1.60	5.87±0.38
Total=33	289.66±5.15$^{*,\&}$	280.33±5.42$^{*,\&}$	198.47±5.69$^{*,\&}$	35.12±1.99$^{*,\&}$	5.66±0.41$^{*,\&}$
AB (12 [12%])					
Sex					
Male (n=4)	254.50±4.20	254.00±10.83	157.95±5.21	45.75±0.95	3.44±0.14
Female (n=8)	264.12±10.43	253.75±7.81	168.25±9.95	45.00±1.30	3.73±0.27
Total=12	260.91±9.82$^{\bullet,\lozenge,\&}$	253.83±8.41$^{\bullet,\lozenge,\&}$	164.81±9.80$^{\bullet,\lozenge,\&}$	45.25±1.21$^{\bullet,\lozenge,\&}$	3.64±0.27$^{\bullet,\lozenge,\&}$
O (18 [18%])					
Sex					
Male (n=2)	273.00±11.31	263.50±9.19	178.80±10.18	41.50±0.70	4.30±0.31
Female (n=16)	276.31±5.70	261.56±25.86	182.50±5.33	40.25±1.06	4.53±0.21
Total=18	275.94±6.11$^{\bullet,\circ,\$,\&}$	261.77±24.40$^{\bullet,\circ,\$,\&}$	182.08±5.71$^{\bullet,\circ,\$,\&}$	40.38±1.09$^{\bullet,\circ,\$,\&}$	4.50±0.23$^{\bullet,\circ,\$,\&}$
Total (100)	287.59±15.99	277.69±19.00	193.44±15.39	38.39±3.84	5.11±0.80
Controls (n=200)					
A (65 [32.5%])					
Sex					
Male (n=32)	205.09±7.96	198.65±5.74	119.95±7.09	45.56±2.97	2.64±0.24
Female (n=33)	205.63±7.16	197.51±8.27	121.43±7.12	44.72±2.34	2.72±0.24
Total=65	205.36±7.51	198.07±7.10	120.70±7.09	45.13±2.68	2.68±0.24
B (75 [37.5%])					
Sex					
Male (n=35)	199.28±9.96	194.94±5.50	109.98±11.52	50.37±6.32	2.22±0.43
Female (n=40)	200.35±5.21	194.47±5.48	110.68±7.31	50.77±4.51	2.20±0.30
Total=75	199.85±7.76	194.69±5.45	110.35±9.45	50.58±5.40	2.21±0.36
AB (20 [10%])					
Sex					
Male (n=13)	140.30±5.05	130.07±3.32	55.88±6.89	58.38±3.70	0.96±0.17
Female (n=7)	140.14±4.22	128.71±3.90	52.68±6.92	61.71±5.93	0.86±0.18
Total=20	140.25±4.66	129.60±3.50	54.76±6.90	59.55±4.74	0.92±0.17
O (40 [20%])					
Sex					
Male (n=39)	166.17±6.54	153.33±5.15	80.56±7.22	54.89±2.51	1.46±0.16
Female (n=1)	166.00±0.00	155.00±0.00	80.00±0.00	55.00±0.00	1.45±0.00
Total=40	166.17±6.46	153.37±5.09	80.55±7.13	54.90±2.47	1.46±0.16
Total (200)	188.95±22.94	181.02±24.86	102.20±22.82	50.57±6.16	2.08±0.64

Tested markers (mean±SD); $^{*,\bullet,\bullet,\lozenge,\circ,\$,\&}$significant at p<0.05, *Compare between A and B within patients group, •Compare between A and AB within patients group, •Compare between A and O within patients group, ◊Compare between B and AB within patients group, ○Compare between B and O within patients group, $Compare between AB and O within patients group, &Compare between total of each blood group in patients and control groups. TGs: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, Tc: Total cholesterol, SD: Standard deviation

the B blood group were more susceptible to hypertension as compared to blood group A and O, whereas AB blood group had less chance of getting hypertension. Another retrospective study was carried out on 23,320 blood donors during a period of 1-year in India showed the B blood group in blood donors was more susceptible to hypertension and obesity [30].

Other reports had shown different outcome and this differences could be explained by the genetic variation for each ethnic group, Kaur [9], and Nishi *et al*. [31] reported incidence of hypertension was the highest in blood group O (43.25%) followed by group A (27.78%), group B (22.62%), and least in group AB (6.35%) and group O illustrated the highest BMI with positive correlation to hypertension.

ABO system and thrombosis

Bezemer and Rosendaal [32] identified ABO blood groups as a new predictive genetic variant for venous thrombosis. "Blood group ABO antigens play important roles in platelet function and are known to be carried by several platelet GPs, for example, GPIb, GPIIb, GPIIIa, and platelet endothelial cell adhesion molecule, GPIIb is an integral component of the GPIIb-GPIIIa fibrinogen receptor complex and blood group A antigen is also expressed uncharacterized platelet proteins (70-90 kD) having electrophoretic motilities closely resembling those of GPIV and GPV both might represent the critical final common pathway for platelet-driven thrombosis in hemostasis and pathologic arterial thrombosis including acute myocardial infarction (MI).

The current study outcome showed group O followed by AB have a protective effect against thrombosis and hypertension then group B and group A illustrated the highest risk for thrombosis and hypertension. This outcome was in agreement with Larsen *et al.* [33], Carpeggiani *et al*. [34] reporting the higher frequency of CAD patients and the higher risk of thrombosis with non-O blood groups suggested a protective anti-atherogenic effect of the blood group O, whereas several clinical studies have shown that individuals of the

Table 3: Mean levels of insulin, RBG, and BMI in type II DM patients and healthy controls versus ABO blood group

Clinical status * blood group * sex	Mean±SD		
	Insulin (μIU/mL)	RBG (mg/dL)	BMI (kg/m^2)
Patients (n=160)			
A (60 [37.5%])			
Sex			
Male (n=20)	10.52±0.40	273.00±20.39	31.50±2.11
Female (n=40)	10.57±0.45	271.77±20.32	32.70±2.00
Total=60	10.55±0.43$^{\&}$	272.18±20.18$^{\&}$	32.30±2.10
B (50 [31.25%])			
Sex			
Male (n=12)	9.53±0.40	268.33±8.59	30.00±1.47
Female (n=38)	9.44±0.52	264.13±11.46	32.76±1.83
Total=50	9.47±0.49*	265.14±10.91*	32.10±2.11*
AB (20 [12.5%])			
Sex			
Male (n=15)	8.36±0.27	222.46±16.76	26.86±0.74
Female (n=5)	8.26±0.06	222.40±16.28	28.80±0.83 3
Total=20	8.33±0.24$^{\bullet,\lozenge,\&}$	222.45±16.21$^{\bullet,\lozenge,\&}$	27.35±1.13$^{\bullet,\lozenge}$
O (30 [18.75%])			
Sex			
Male (n=23)	8.23±0.38	250.86±10.91	29.17±1.52
Female (n=7)	8.36±0.32	246.71±9.92	29.28±1.11
Total=30	8.26±0.37$^{\bullet,\circ}$	249.90±10.67$^{\bullet,\$}$	29.20±1.42$^{\bullet,\circ,\$}$
Total (160)	9.51±1.03	259.58±22.37	31.03±2.61
Controls (n=200)			
A (65 [32.5%])			
Sex			
Male (n=32)	4.78±0.26	137.87±1.69	25.50±1.81
Female (n=33)	4.80±0.35	139.12±1.96	26.33±1.67
Total=65	4.79±0.31	138.50±1.92	25.92±1.177
B (75 [37.5%])			
Sex			
Male (n=35)	4.12±0.31	132.42±7.68	23.57±2.52
Female (n=40)	4.12±0.72	134.55±8.88	24.77±2.17
Total=75	4.12±0.57	133.56±8.36	24.21±2.40
AB (20 [10%])			
Sex			
Male (n=13)	3.90±0.32	95.69±6.06	20.23±1.42
Female (n=7)	3.50±0.78	95.14±3.67	21.57±1.98
Total=20	3.76±0.54	95.50±5.24	20.70±1.71
O (40 [20%])			
Sex			
Male (n=39)	4.26±0.58	132.38±2.90	24.17±1.07
Female (n=1)	4.15±0.00	130.00±0.00	24.00±0.00
Total=40	4.25±0.58	132.32±2.89	24.17±1.05
Total (200)	4.33±0.60	131.11±13.39	24.41±2.41

Tested markers (mean±SD); $^{*,\bullet,\bullet,\lozenge,\circ,\$,\&}$significant at p<0.05, *Compare between A and B within patients group, •Compare between A and AB within patients group, •Compare between A and O within patients group, $^{\lozenge}$Compare between B and AB within patients group, $^{\circ}$Compare between B and O within patients group, $^{\$}$Compare between AB and O within patients group, $^{\&}$Compare between total of each blood group in patients and control groups, RBG: Random blood glucose, BMI: Body mass index, DM: Diabetes mellitus, SD: Standard deviation

A phenotype blood group are the more susceptible to cardiovascular disease [35]. In British men, the incidence of ischemic heart disease is higher in patients with blood group A [36]. Likewise, in the Hungarian population, again blood group A is the more common in patients with chronic heart disease [37]. Reza [38] reported A and B blood groups are one of the genetically based factors of risk in the link of atherosclerosis pathogenesis.

Blood group O may provide protection for cardiovascular diseases including; myocardial, cerebral, and peripheral vascular thrombosis while individuals with an A or B blood type have increased risk of venous thromboembolism and MI [39]. Tarjan *et al*. [37] concluded that blood group A was the more frequent, and the blood group O was less frequent among the patients with positive coronary angiography. Sex has no significant effect in the current study while Stakisaitis *et al*. [28] found that the blood group B can be related with coronary atherosclerosis in women, and the blood group O can possibly serve as a protective anti-atherogenic factor in women which is in agreement with the results pattern.

Interestingly, ABO blood group is a key determinant of coagulation factor VIII and vWF plasma concentrations [10]. This finding of O protective effect against thrombosis might be explained as blood group O have about 25% less factor VIII (F VIII) and vWF in their plasma result in excess bleeding [10,33]. These factors have a relationship with hypercholesterolemia which in turn has a relationship with diabetes [40].

Gonzales *et al*. [41] explained the effect of testosterone hormone that induces the production of TXB_2 in animals. The current study showed no difference in human between male and female in TXB_2 levels (table IV) and all other thrombotic factors which postulating no induction effect of testosterone on TBX_2 production in human.

In human studies, 11-dehydro-TX B2 levels are used to indirectly measure TXA_2 production as TXA_2 is very unstable in aqueous solution, since it is hydrolyzed within about 30 seconds to the biologically inactive TX B_2. Due to its very short half-life, TXA_2 primarily functions as an autocrine or paracrine mediator in the nearby tissues surrounding its site of production. Most work in the field of TXA_2 is done instead with synthetic analogs such as U46619 and I-BOP. Group O is lowering the vasoconstrictor TXA_2 (TXB_2) level and increasing the vasodilator prostacyclin and this could explain the protective effect of O group [42].

Few reports were in contrary partly to the current represented results, Meade *et al*. [43] reported significant higher incidence of CVD in blood group AB as compared to those of B and O Skaik [44] found that group A was the most common (57%), and the group O was the second (30.5%) among the MI patients in Gaza Strip of Palestine. Whereas Biswas *et al*. [45] showed blood group O is higher in CAD than other ABO blood groups.

ABO blood groups and type II DM

Non-insulin-dependent DM (type 2) is characterized by elevated insulin levels that are ineffective in normalizing blood sugar levels [14].

Koley [46] reported that there is no association between ABO blood groups and DM**,** while a GWAS showed that genetic variants in the ABO locus were associated with inflammation and type 2 DM risk [47]. It is interesting to note that the ABO locus influences pepsinogen secretion [48], a marker linked to insulin gene on chromosome 11 [49].

The current study outcome showed that group A has a risk factor on diabetic patients by increased levels of insulin and RBG, while AB group showed a protective effect whereas B and O blood groups showed insignificant effect. Several studies were in agreement with the current study outcome, a significant excess of blood group A among male diabetics, such as a combined series from Lancashire, Cheshire, and Oxford [50]. McConnell *et al*. [51] concluded that an increased frequency of A blood group among diabetic patients.

In contrary to the current study, Qi *et al*. [47] showed that blood group B showing a decreased risk compared with blood group O in patients with DM type 2. Kamil *et al*. [52] reported a significant lower percentage of O and A blood groups among diabetic patients, which means a negative association with these blood groups while blood group B was prevalent at a high percentage among patients with DM type II**.**

CONCLUSION

Blood group AB is protective against diabetes, thrombosis, and hyperlipidemia, blood group O is protective against hypertension and cardiovascular diseases while blood group B followed by A are

Table 4: Mean levels of prothrombin time, aPPT, levels of prostacyclin (PGI_2), and TXB_2 in hypertensive patients and healthy controls versus ABO blood group

Clinical status * blood group * sex	Mean±SD			
	PT (seconds)	aPPT (seconds)	Plasma 2,3-dinor-6-keto $PGF_{1\alpha}$ (pg/mL)	Plasma 11-dehydro-TXB_2 (pg/mL)
Patients (n=166)				
A (50 [30.1%])				
Sex				
Male (n=41)	16.09±2.23	38.21±4.05	1.05±0.18	2.27±0.27
Female (n=9)	18.88±1.45	33.88±7.75	1.06±0.18	2.15±0.46
Total=50	16.60±2.36	37.44±5.10	1.05±0.17$^{\&}$	2.25±0.31
B (81 [48.7%])				
Sex				
Male (n=67)	13.84±2.26	29.01±4.26	0.92±0.34	3.08±0.53
Female (n=14)	11.07±1.79	28.21±7.56	1.41±0.34	2.56±0.78
Total=81	13.36±2.42$^{*,\&}$	28.87±4.94$^{*,\&}$	1.00±0.38*	2.99±0.61$^{*,\&}$
AB (23 [13.8%])				
Sex				
Male (n=9)	22.22±1.30	44.44±4.03	2.31±0.42	2.13±0.16
Female (n=14)	22.07±1.54	42.42±1.50	2.30±0.30	2.08±0.13
Total=23	22.13±1.42$^{\blacklozenge,\lozenge,\&}$	43.21±2.87$^{\blacklozenge,\lozenge,\&}$	2.30±0.34$^{\blacklozenge,\lozenge,\&}$	2.10±0.14$^{\lozenge}$
O (12 [7.2%])				
Sex				
Male (n=2)	25.50±0.70	51.00±1.41	3.16±0.07	1.17±0.02
Female (n=10)	23.00±1.49	51.70±1.49	3.20±0.16	1.14±0.07
Total=12	23.41±1.67$^{\bullet,\circ,\$,\&}$	51.58±1.44$^{\bullet,\circ,\&}$	3.19±0.14$^{\bullet,\circ,\$,\&}$	1.15±0.06$^{\bullet,\circ,\$,\&}$
Total=166	16.28±4.20	35.08±8.39	1.36±0.74	2.51±0.71
Controls (n=174)				
A (65 [37.3%])				
Sex				
Male (n=32)	12.14±1.10	31.96±4.35	1.96±0.19	1.98±0.17
Female (n=33)	12.14±0.68	31.24±3.78	1.92±0.22	1.94±0.23
Total=65	12.14±0.91	31.60±4.05	1.94±0.21	1.96±0.20
B (49 [28.1%])				
Sex				
Male (n=21)	11.64±1.41	23.23±6.22	1.52±0.23	2.13±0.56
Female (n=28)	11.77±1.34	22.21±2.02	1.53±0.21	2.23±0.56
Total=49	11.71±1.36	22.65±4.32	1.53±0.21	2.19±0.56
AB (20 [11.4%])				
Sex				
Male (n=13)	12.88±1.17	33.84±2.99	2.28±0.13	1.79±0.18
Female (n=7)	12.72±0.80	34.28±7.75	2.71±0.64	1.71±0.37
Total=20	12.83±1.04	34.00±2.84	2.43±0.45	1.76±0.25
O (40 [22.9%])				
Sex				
Male (n=39)	13.56±0.78	37.53±2.15	3.23±0.24	1.31±0.30
Female (n=1)	14.00±0.00	38.00±0.00	3.12±0.00	1.30±0.00
Total=40	13.57±0.78	37.55±2.12	3.23±0.24	1.31±0.29
Total=174	12.43±1.25	30.72±6.62	2.18±0.68	1.85±0.48

Tested markers (mean±SD); $^{*,\blacklozenge,\bullet,\lozenge,\circ,\$,\&}$significant at p<0.05, *Compare between A and B within patients group, $^{\blacklozenge}$Compare between A and AB within patients group, $^{\bullet}$Compare between A and O within patients group, $^{\lozenge}$Compare between B and AB within patients group, $^{\circ}$Compare between B and O within patients group, $^{\$}$Compare between AB and O within patients group, $^{\&}$Compare between total of each blood group in patients and control groups, aPPT: Activated partial prothrombin time, PT: Prothrombin time, SD: Standard deviation, TXB_2: Thromboxane B_2, PGF1α: Prostaglandin F1α

Table 5a: Illustration of ABO groups effect on all studied parameters

ABO group	Insulin level	RBS (mg/dL)	BMI (Kg/m^2)	aPPT (seconds)	PT (seconds)	Plasma 2,3-dinor-6-keto PGF1α (pg/mL)	Plasma 11-dehydro-TXB_2 (pg/mL)	Tc (mg/dL)	TGs (mg/dL)	LDL/HDL ratio (%)
A	↑	↑	↑	↓	N	↓	N	↑	↑	↑
B	N	N	↑	↓	↓	N	↑	↑	↑	↑
AB	↓	↓	↓	↑	↑	↑	N	↓	↓	↓
O	N	N	↓	↑	↑	↑	↓	↓	↓	↓

N: Non-significant effect, RBS: Random blood sugar, BMI: Body mass index, aPPT: Activated partial prothrombin time, TXB_2: Thromboxane B_2, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, Tc: Total cholesterol, TGs: Triglycerides, PT: Prothrombin time, PGF1α: Prostaglandin F1α

Table 5b: ABO groups' correlation with all studied diseases

ABO group	Diabetes	Cardiovascular diseases		
		Thrombosis	Hyperlipidemia	Hypertension (%)
A	R	R	R	30
B	N	R	R	49
AB	P	P	P	14
O	N	P	P	7

R: Risk in both genders, P: Protective, N: Non-significant effect

risk factors for Hypertension and cardiovascular disease and blood group A is a risk factor for diabetes. All the previous ABO blood groups effects in correlation to the investigated diseases might be an ethnic-dependent.

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AUTHORS CONTRIBUTION

Both authors were involved and contributed to the proposal design, conception and design of the manuscript, analyzed, collected, assembled and interpreted the data, provided the study material, intellectual content, graphics design, involved in manuscript writing, final approval of all parts of the manuscript.

CONFLICT OF INTEREST AND FINANCIAL STATEMENTS

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