CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
http://doi.org/10.5281/zenodo.3370278

Available online at: http://www.iajps.com *Research Article*

RELATION OF CORONARY ARTERY DISEASES WITH ABO SYSTEM AND LEWIS BLOOD PHENOTYPES

[1]Dr Maria Shabbir, [2]Dr Saeeda Bano, [3]Dr Noor Ul Ain

[1]MBBS, DCP, M.Phil Haematology, Maroof International Hospital Islamabad, [2]MBBS, PGD Nutrition, Ms. SLP Islamic International Medical College Riphah, [3]MBBS Islamic International Medical College Riphah.

Article Received: June 2019 **Accepted:** July 2019 **Published:** August 2019

Abstract:

Objective: *To evaluate the pattern and relationship of ABO and Lewis blood group phenotypes in patients with coronary heart disease.*

Study Design: *An analytical case-control study.*

Place and duration: *In the Department of Medicine and Cardiology, Benazir Bhutto Hospital Rawalpindi for one year duration from March 2017 to March 2018.*

Methods: *In this study total 187 CAD clinically confirmed patients with sex and age were compared to 187 healthy controls were included. To determine the relationship of CAD with risk factors; Lewis antigen typing and ABO grouping were determined. Using SPSS version 21.0; statistical analysis was done and categorical variables were recorded in percentages.*

Results: *In the control group (41.2%) the most common blood group was O blood group, followed by 33.2% of B group, 21.9% were of A and 3.7% were determined as AB. In CAD patients; the group O prevalence was nearly same to that of the control group, but the incidence of non-O groups showed mild rise in CAD cases; the AB group frequency in these subjects was relatively low compared to the control group. The Le (a-b-) phenotype prevalence was found to be 32.5%. We noted that hypertension, smoking, dyslipidemia, diabetes mellitus are the associated with risk factors noted in 94.1% of the cases.*

Conclusion: *This study showed that ABO blood group did not show important relationship with coronary artery disease, but ABO group has strong relationship with risk factors such as smoking, dyslipidemia and hypertension. In addition, Le (a-b-) phenotype showed a significant relationship with coronary artery disease and risk factors such as smoking, dyslipidemia and hypertension.*

Key Words: *Ischaemic disease, Lewis negative phenotype, ABO blood group system.*

Corresponding author:

Dr. Maria Shabbir,

MBBS, DCP, M.Phil Haematology, Maroof International Hospital Islamabad.

QR code

Please cite this article in press Maria Shabbir et al., ***Relation Of Coronary Artery Diseases With Abo System And Lewis Blood Phenotypes.,*** *Indo Am. J. P. Sci, 2019; 06[08].*

INTRODUCTION:

Blood group antigens of the Lewis and ABO systems are not only expressed on the red blood cell membrane (RBC), but are also expressed on the surface of platelets, vascular endothelium, sensory neurons and epithelials. Lewis (Le) antigens are mainly found in secretions and plasma and adsorbed in the red blood cell membrane[1-2]. Studies report that blood group A individuals are more susceptible to cardiovascular disease[3]. The most important of these was the Framingham study, which reported that individuals with phenotype "A" were more susceptible to CAD. Wazirali H et al. suggested that group A blood group increased the risk of CAD regardless of conventional risk factors[4]. Some Pakistani studies have also reported that the rate of coronary artery disease in the blood group A in North Bengal is higher than in other blood groups. Chen Z et al., in 17 studies meta-analysis, showed that the CAD risk in A blood group was slightly higher and lesser in O blood group[5]. In contrast, Garg P et al. a strong relationship between blood group B and CAD was observed. India, Gujarat, Sahita P et al did not observe a relationship between blood type and CAD after excluding patients with risk factors[6]. The Le (a-b-) phenotype prevalence was found to be significant and almost 2.5 times higher in patients with CAD compared to the control group[7]. Salomaa V et al., It was observed that the internal thickness of the carotid was slightly higher in subjects with negative Lewis phenotype than those with positive Lewis phenotype. Lewis blood group (a-b-) has been reported to be related with hypercholesterolemia, diabetes mellitus and insulin resistance conditions, which are considered high risk factors for CAD. The relationship between subclinical carotid atherosclerosis and Lewis genotype was reported by Cakir B et al., Who reported that there was no significant statistically relationship between subclinical atherosclerosis and Lewis genotype[8].

MATERIALS AND METHODS

This analytical case-control study was held in the Department of Medicine and Cardiology, Benazir Bhutto Hospital Rawalpindi for one year duration from March 2017 to March 2018.

The inclusion criteria included patients with the diagnosis of CAD based on electrocardiographic changes of ischemia such as chest pain, ST elevation, and related risk factors such as smoking history and hypertension among patients aged 20-65 years, diabetes mellitus and changes in lipid profile. Only patients who underwent percutaneous transluminal coronary angioplasty in the cardiology department of the institute and showed angiographically positive results were included in the study. Exclusion criteria were patients over 65 years of age who had other comorbid diseases such as malignancy and pregnant women and did not want to participate in the study. In 1945, the same age and sex were taken as controls for healthy blood donors who could donate blood according to the exclusion and inclusion criteria of the Pharmaceutical and Cosmetic Rules. After obtaining the written approval of each subject, 3 ml of blood was taken from each CAD patient in blood donors in an ethylenediaminetetraacetic acid (EDTA) anticoagulant tube. Repeated blood sampling from the same subject was prevented by personally verifying the demographic profile of the patient, including the full name, age, address, hospital registration number, and collecting the required amount of blood. ABO blood grouping was performed in accordance with the Department's Standard Operating Procedures (SOP). Commercially available monoclonal blood group antisera were used for direct grouping; for reverse grouping, A, B and O cells pooled in a 5% pool prepared according to SOP were used. Lewis antigen typing was performed by a method of colon agglutination technology using Lea, Leb monoclonal antiserum (Ortho Clinical Diagnostics, High Wycombe, UK) in an inverted diluent cassette according to instructions manual.

Using SPSS version 21.0; statistical analysis was done. Descriptive statistics for categorical variables were calculated by calculating the frequency (percentage) in each category. The comparison of categorical data between the relation of Lewis phenotypes and ABO in clinically CAD confirmed patients was performed using the chi-square test. The incidence was proportional to the 95% confidence interval (CI). All statistical analyzes were performed at 5% significance level and $p < 0.05$ was considered significant.

RESULTS:

During the study, 187 patients diagnosed with CAD were investigated for the association between CAD and Lewis phenotypes and ABO blood grouping, and 187 healthy volunteer blood donors who participated in the study recognized the age and sex control group. There were 166 (89%) males and 21 (11%) females in both CAD and control groups.

Blood groups	Cases		Control		p-value*
	Number	Percentage	Number	Percentage	
O	77	41.2%	80	42.8%	0.39
B	62	33.2%	58	31.0%	
A	41	21.9%	35	18.7%	
AB	7	3.7%	14	7.5%	
Total	187	100%	187	100%	

[Table/Fig-1]: Distribution of blood groups in CAD cases and controls.
*by chi-square test

[Table / Figure 1] shows ABO blood groups distribution between cases and CAD controls. The most common group was Group O, followed by Group B in both the case and control groups, and there was no significant relationship between CAD and controls (p value = 0.39).

Lewis	Cases		Controls		p-value
Phenotype	Number	Percentage	Number	Percentage	
Le (a-b-)	115	61.5%	61	32.6%	0.001*
Le (a-b+)	69	37.0%	125	66.9%	
Le (a+b-)	2	1.0%	1	0.5%	
Le (a+b+)	1	0.5%	0	0	
Total	187	100%	187	100%	

[Table/Fig-2]: Distribution of Lewis phenotype with CAD cases and controls.
*Significant by chi-square test

[Table / Figure 2] shows the distribution of Lewis phenotypes in CAD cases and controls. Le (ab-) was the most common phenotype (61.5%), followed by Le (ab +) (37%) and Le (ab +) was the most common phenotype (66.9%) and Le (ab-). (32.6%) in the controls. Le (a-b-) phenotype had a significant relationship with patients with CAD.

Blood groups	Hyperten-sion n (%)	Diabetes n (%)	Dys-lipidemia n (%)	Smoking n (%)	Family History of CAD n (%)
O	28 (38.4)	22 (40)	20 (40)	66 (43.4)	14 (28)
B	22 (30.1)	21 (38.2)	8 (16)	53 (34.9)	5 (10)
A	22 (30.1)	11 (20)	22 (44)	26 (17.1)	31 (62)
AB	1 (1.4)	1 (1.8)	0 (0)	7 (4.6)	0 (0)
Total (% among 187)	73 (39.03%)	55 (29.41%)	50 (26.73%)	152 (81.28%)	50 (26.73%)
Le (a-b-)	40 (54.8)	45 (81.8)	38 (76)	100 (65.8)	34 (68)
Le (a-b+)	32 (43.8)	10 (18.2)	12 (24)	52 (34.2)	16 (32)
Le (a+b-)	1 (1.4)	0 (0)	0 (0)	0 (0)	0 (0)
Le (a+b+)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total (% among 187)	73 (39.03%)	55 (29.41%)	50 (26.73%)	152 (81.28%)	50 (26.73%)

[Table/Fig-3]: Frequency of various risk factors with ABO and Lewis blood groups in cases.

[Table / Figure 3] shows the frequency of several risk factors in CAD patients with ABO and Lewis blood group. Smoking (81.2%) followed by hypertension (39%) was the most common risk factor for CAD.

Blood groups	CAD cases with hypertension n (%)	CAD cases without hypertension n (%)	p-value
O	28 (38.4)	49 (43)	0.53
B	22 (30.1)	40 (35)	0.48
A	22 (30.1)	19 (17)	0.02*
AB	1 (1.4)	6 (5)	0.33
Le (a-b-)	40 (54.8)	75 (65.8)	0.13
Le (a-b+)	32 (43.8)	37 (32.5)	0.11
Le (a+b-)	1 (1.4)	1 (0.8)	0.74
Le (a+b+)	0 (0)	1 (0.8)	0.42

[Table/Fig-4]: Association of hypertension between ABO and lewis blood groups.
*Significant by chi-square test

[Table / Figure 4] shows a significant hypertension relationship as a risk factor for CAD patients with blood group A (p value = 0.02) and no significant relationship with Lewis blood groups.

Blood groups	CAD cases with diabetes mellitus n (%)	CAD cases without diabetes mellitus n (%)	Total n (%)	p-value
O	22 (40)	55 (41.7)	77 (41)	0.83
B	21 (38.2)	41 (31)	62 (33)	0.34
A	11 (20)	30 (22.7)	41 (22)	0.68
AB	1 (1.8)	6 (4.5)	7 (4)	0.37
Le (a-b-)	45 (81.8)	70 (53)	115 (61.4)	<0.001*
Le (a-b+)	10 (18.2)	59 (44.7)	69 (37)	0.001*
Le (a+b-)	0 (0)	2 (1.5)	2 (1.1)	0.35
Le (a+b+)	0 (0)	1 (0.8)	1 (0.5)	0.51

[Table/Fig-5]: Association of diabetes mellitus between ABO and lewis blood groups.
*Significant by chi-square test

[Table / Figure 5] shows that there is no significant relationship with diabetes mellitus for CAD patients with ABO blood groups, but it is significant with the Lewis Le (a-b-) and Le (a-b +) phenotype.

Blood groups	CAD cases with dyslipidemia n (%)	CAD cases without dyslipidemia n (%)	Total n (%)	p-value
O	20 (40)	57 (42)	77 (41)	0.84
B	08 (16)	54 (39)	62 (33)	0.003*
A	22 (44)	19 (13.9)	41 (22)	<0.001*
AB	0 (0)	7 (5.1)	7 (4)	0.10
Le (a-b-)	38 (76)	77 (56.2)	115 (61.4)	0.014*
Le (a-b+)	12 (24)	57 (41.5)	69 (37)	0.027*
Le (a+b-)	0 (0)	2 (1.5)	2 (1.1)	0.39
Le (a+b+)	0 (0)	1 (0.8)	1 (0.5)	0.54

[Table/Fig-6]: Association of dyslipidemia between ABO and lewis blood groups.
*Significant by chi-square test

[Table / Figure 6] shows a significant association of dyslipidemia as a risk factor for subjects with A and B blood groups and also with the Lewis Le (a-b-) and Le (a-b +) phenotype.

Blood groups	CAD cases with smoking n (%)	CAD cases without smoking n (%)	Total n (%)	p-value
O	66 (43.4)	11 (31.4)	77 (41)	0.19
B	53 (34.9)	09 (25.7)	62 (33)	0.30
A	26 (17.1)	15 (42.9)	41 (22)	0.001*
AB	7 (4.6)	0 (0)	7 (4)	0.19
Le (a-b-)	100 (65.8)	15 (42.8)	115 (61.4)	0.01*
Le (a-b+)	52 (34.2)	17 (48.6)	69 (37)	0.11
Le (a+b-)	0 (0)	2 (5.7)	2 (1.1)	0.003*
Le (a+b+)	0 (0)	1 (2.9)	1 (0.5)	0.03*

[Table/Fig-7]: Association of smoking between ABO and lewis blood groups.
*Significant by chi-square test

[Table / Figure 7] shows that smoking has a significant relationship as a risk factor in patients with CAD of blood group A, but shows that it is important with the exception of the Lewis Le (ab +) phenotype. Three phenotypes Multivariate logistic regression analysis showed that the Lewis phenotype was independently related with increase CAD risk (Ratio ratio: 1.71; 95% CI: 1.50-1.89) [Table / Figure 8].

Variables	Odds Ratio (95% CI)	p-value
ABO blood group	0.16 (0.09-0.20)	0.713
Lewis phenotype	1.71 (1.50-1.89)	<0.001*
Hypertension	1.51 (1.26-1.87)	<0.001*
Diabetes	1.34 (1.11-1.72)	<0.001*
Dyslipidemia	1.50 (1.23-1.96)	<0.001*
Smoking	1.48 (1.02-1.76)	<0.001*

[Table/Fig-8]: Multivariable logistic regression analysis for predicting risk factors for CAD.
*significant by Multivariable Logistic Regression Analysis

DISCUSSION:

The present aim was to investigate the association and pattern of Lewis phenotypes and ABO blood grouping in patients with clinically confirmed CAD[9-10]. In this study, the most common blood group was O in 41.2% of cases, followed by B group (33.2%), A group (21.9%) and AB group (3.7%). The blood group O prevalence in patients with CAD was nearly same to that observed in controls, but moderately, the non-O 'group frequency, ie, groups A, B, showed a slight increase in patients with CAD. The AB blood group frequency in these subjects was lower than in the control group[11]. A study by Sharif S et al. In Lahore, Punjab Institute of Cardiology showed that subjects with blood group A had a significantly higher risk of developing CAD than other blood groups[12]. A study by Whincup PH et al. noted that CAD incidence was higher in A blood group subjects than in non-A subjects. A study by Garg P et al. Reported a significant relationship between HR and blood group B, where Banerjee S et al. showed a high rate of CAD in blood group A[13]. The association of CAD with ABO blood group was supported by evidence that high levels of von-willebrand factor (vWF) -Factor VIII was a risk factor for CAD. Blood group O individuals had approximately 25% lower plasma factor factor VIII and vWF levels in non-O blood groups than other groups at higher risk of thrombosis and CAD. The risk factors such as hypertension, smoking, dyslipidemia and diabetes mellitus were associated with CAD in

94.1% of cases. Sharif S et al. showed that the prevalence of general hypertension was higher with 58.5% compared with 53.5% of diabetes[14]. Of the 187 patients in this study group, 73 (39.0%) had hypertension with a significant association with blood group A, and 55 (29.4%) had associated type II diabetes mellitus, but did not show a significant relationship with the groups. ABO blood. Sayed EL and Amine HC have shown that hypertension is more common in blood group B and then in blood group A[15]. They observed that blood type O protects against hypertension and blood groups A and B protect against diabetes and hyperlipidemia. Chandra T and Gupta A showed that people in blood group B were more susceptible to hypertension. In contrast to previous studies, hypertension was observed more in blood group O (38.4%).Blood group A has been reported to show high levels of total cholesterol (CT) and low density lipoprotein (LDL). In many studies, high CT, triglycerides (TG), LDL and low high density lipoproteins (HDL), O and finally AB groups were found to be low in blood groups A and B. This study showed a significant relationship with blood groups A and B. In a study by Sharif S et al., Smoking was observed to be 54%. As in this study, 81.2% were observed. Lewis antigens play a well-defined role in selectin-mediated cell adhesion events and in defense against inflammation and infection. In the absence of these antigens, inflammation and chronic infection, as in Le (a-b-), contribute to the multifactorial pathogenesis of coronary heart disease events. This may be a reason for obtaining Le (a-b-) CAD in existing patients.

CONCLUSION:

This study results showed a slight increase in the susceptibility of individuals in blood group A and B to CAD compared to the control group. However, this training did not validate a strong relation of ABO blood group with CAD. However, the study demonstrated a significant association of ABO blood group with risk factors such as smoking, dyslipidemia and hypertension. This study also demonstrated a substantial relationship of Le (a-b-) phenotype with CAD and risk factors such as smoking, dyslipidemia and hypertension. Detection of the Lewis phenotype may help to take primary prevention measures against CAD.

REFERENCES:

1. Enevold, C., C. H. Nielsen, D. Molbo, R. Lund, K. Bendtzen, N-E. Fiehn, and P. Holmstrup. "Lewis and AB0 blood group-phenotypes in periodontitis, cardiovascular disease, obesity and stroke." *Scientific reports* 9, no. 1 (2019): 6283.
2. Mjali, Ahmed, Anwar Sheikha, Hazha Abdullah Amin, Mohammed Jawad Al-Anssari, Azeez Aljawdah, Zahraa Dheyaa, and Saja Khudhair Abbas. "Association between Female Breast Cancer and Different ABO Blood Groups & Rh Factor in the Sulaymaniyah Province of Iraqi Kurdistan." *Indian Journal of Public Health Research & Development* 10, no. 6 (2019).
3. Sliz, Eeva, Marita Kalaoja, Ari Ahola-Olli, Olli Raitakari, Markus Perola, Veikko Salomaa, Terho Lehtimäki et al. "Genome-wide association study identifies seven novel loci associating with circulating cytokines and cell adhesion molecules in Finns." *Journal of Medical Genetics* (2019): jmedgenet-2018.
4. House, Andrew A., Christoph Wanner, Mark J. Sarnak, Ileana L. Piña, Christopher W. McIntyre, Paul Komenda, Bertram L. Kasiske et al. "Heart failure in chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference." *Kidney international* 95, no. 6 (2019): 1304-1317.
5. Pisk, Sandra Vuk, Tomislav Vuk, Ena Ivezić, Irena Jukić, Jasna Bingulac-Popović, and Igor Filipčić. "ABO blood groups and psychiatric disorders: a Croatian study." *Blood Transfusion* 17, no. 1 (2019): 66.
6. Lewis, Meghan, Ira Shulman, Jay Hudgins, Ernest E. Moore, and Kenji Inaba. "Essentials of emergency transfusion—The complement to stop the bleed." *Journal of Trauma and Acute Care Surgery* 87, no. 2 (2019): 420-429.
7. Schoeman, Elizna M., Eileen V. Roulis, Maree A. Perry, Robert L. Flower, and Catherine A. Hyland. "Comprehensive blood group antigen profile predictions for Western Desert Indigenous Australians from whole exome sequence data." *Transfusion* 59, no. 2 (2019): 768-778.
8. Yue, Y., Sun, Q., Man, C. and Fu, Y., 2019. Association of the CYP4V2 polymorphism rs13146272 with venous thromboembolism in a Chinese population. *Clinical and experimental medicine*, *19*(1), pp.159-166.
9. Vila-Caballer, Marian, José M. González-Granado, Virginia Zorita, Yafa N. Abu Nabah, Carlos Silvestre-Roig, Alberto del Monte-Monge, Pedro Molina-Sánchez et al. "Disruption of the CCL1-CCR8 axis inhibits vascular Treg recruitment and function and promotes atherosclerosis in mice." *Journal of molecular and cellular cardiology* 132 (2019): 154-163.

10. Lewis, Gavin A., Erik B. Schelbert, Josephine H. Naish, Emma Bedson, Susanna Dodd, Helen Eccleson, Dannii Clayton et al. "Pirfenidone in Heart Failure with Preserved Ejection Fraction—Rationale and Design of the PIROUETTE Trial." *Cardiovascular drugs and therapy* (2019): 1-10.
11. Ahmed, S.G., Ibrahim, U.A. and Kagu, M.B., 2019. Opioid dependence among people with haemophilia in a low-resource tropical setting: prevalence and risk factors in northern Nigeria. *The Journal of Haemophilia Practice*, *6*(1), pp.19-28.
12. Jia, Q., Han, Y., Huang, P., Woodward, N.C., Gukasyan, J., Kettunen, J., Ala-Korpela, M., Anufrieva, O., Wang, Q., Perola, M. and Raitakari, O., 2019. Genetic Determinants of Circulating Glycine Levels and Risk of Coronary Artery Disease. *Journal of the American Heart Association*, *8*(10), p.e011922.
13. Rietveld, I.M., Lijfering, W.M., le Cessie, S., Bos, M.H., Rosendaal, F.R., Reitsma, P.H. and Cannegieter, S.C., 2019. High levels of coagulation factors and venous thrombosis risk: strongest association for factor VIII and von Willebrand factor. *Journal of Thrombosis and Haemostasis*, *17*(1), pp.99-109.
14. Lefaucheur, C., Viglietti, D., Bouatou, Y., Philippe, A., Pievani, D., Aubert, O., Van Huyen, J.P.D., Taupin, J.L., Glotz, D., Legendre, C. and Loupy, A., 2019. Non-HLA agonistic anti-angiotensin II type 1 receptor antibodies induce a distinctive phenotype of antibody-mediated rejection in kidney transplant recipients. *Kidney international*.
15. Eren, C. and Çeçen, S., 2019. An Analysis on the Association Between ABO and Rh Blood Groups with Obesity. *Proceedings of the National Academy of Sciences, India Section B: Biological Sciences*, *89*(3), pp.1095-1100.