# ГОСТУВАЩИ АВТОРИ
# GUEST AUTHORS

## THE ASSOCIATIONS OF ABO BLOOD GROUP TYPE AND COMMON BIOCHEMICAL PARAMETERS WITH CHOLESTEROLEMIA AND HYPERGLYCEMIA IN PERSONS WITH CONNECTIVE TISSUE PATHOLOGY

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***Abstract. Introduction.*** *The studies demonstrated the associations of ABO blood group type with numerous diseases. Nevertheless, very few researches are devoted to searching for possible associations of blood group type with obesity and diabetes mellitus. The study aimed to find the frequency of ABO blood group types with hypercholesterinemia and hyperglycemia in patients with connective tissue pathologies.* ***Material and methods.*** *Serum cholesterin, glucose and usual biochemical parameters were measured by standard biochemical methods. Bacterial investigation of the synovial fluid was performed for 23 patients. Blood group type was defined by the direct method of agglutination using standard IgM anti-A and anti-B antibodies. Thirty patients (17 men and 13 women) aged 62.0 ± 2.1 years with gonarthrosis and coxarthrosis were included in the study. Detection of autoimmune lymphocytotoxic and granulocytotoxic antibodies and the reaction of leukocyte migration inhibition with tissue, bacterial and fungal antigens were performed for all patients.* ***Results.*** *A blood group type appeared to be predisposed to obesity (40%). The O blood group was the least suspected of hypercholesterolemia (40%). A and B blood group types were more predisposed to hyperglycemia than O blood group type (40%, 26.6%, 33.3%, respectively). Persons with the O blood group appeared to be of the highest frequency among the patients with normal glucose levels (33.3%). Persons with hyperlipidemia demonstrated leukocyte migration inhibition to Escherichia coli, Proteus vulgaris, Staphylococcus aureus, and Streptococcus pyogenes. In persons with hyperlipidemia, an appearance of Pseudomonas aeruginosa and Candida lusitaniae growth, various types of Staphylococci along with an increased frequency of Staphylococcus aureus, Bacillus subtilis, Acinetobacter, and increased growth of Escherichia coli have been found. Patients with hyperglycemia demonstrated leukocyte migration enhancement to Streptococcus pyogenes, Pseudomonas aeruginosa, Escherichia coli, and Staphylococcus aureus. Persons with hyperglycemia demonstrated an appearance of Candida lusitaniae, Staphylococcus hominis, Acinetobacter and Bacillus subtilis in bacterial findings from wounds, as well as increased frequency of Staphylococcus aureus and different types of Staphylococci.* ***Conclusions.*** *A blood group was found to be predisposed to obesity, whereas the O blood group type appeared to be the least suspected of hypercholesterolemia. A and B blood group types have been shown to be predisposed to hyperglycemia. Hypercholesterinemia was associated with leukocyte migration inhibition to Escherichia coli and Proteus vulgaris, whereas hyperglycosemia – with leukocyte migration enhancement to Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Streptococcus pyogenes.*

***Key words:*** *A antigen, B antigen, blood, cholesterin, glucose*

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### INTRODUCTION

Numerous studies demonstrated the associations of ABO blood group type with diseases, such as cancer, cardiovascular diseases, infections and hematologic disorders, cognitive disorders, circulatory diseases, metabolic diseases, and malaria [1]. ABO blood groups were primarily associated with cardiovascular outcomes. Compared with individuals with blood group O, blood groups A and B were associated with increased risk for thromboembolic events and decreased risk for hypertension [2]. Total cholesterol was significantly higher in non-O subjects than in the O group carriers [3]. The researchers observed a greater proportion of subjects carrying the non-O groups (73.4 %) in patients with cardiovascular diseases compared to subjects without cardiovascular diseases. The au-

thors declared the ABO blood group to represent a novel risk factor in subjects with family hypercholesterinemia that is often known by the patient and could be used to further stratify cardiovascular risk in this population of patients. The association between the identified longevity-associated ABO variants and better health lipid profile was elucidated. Thus the authors reported that the findings can help maintain normal lipid metabolic phenotypes in the longevity population [4]. Few research pieces are devoted to the possible associations of blood group type with obesity and diabetes mellitus. The A blood group has been revealed to be a risk factor for IHD in individuals with type 1 diabetes and microalbuminuria [5]. The relations of ABO blood group type with disturbances of glucose and lipid metabolism are of current interest since glycosyltransferases necessary for the metabolism of the glucose pathway are the key factors for the synthesis of blood group antigens. The link between the ABO blood type and glucose metabolism is intervened by the glycosyltransferase activity.

The previous study examined the validity of a blood-type diet in overweight adults. After a 6-month dietary intervention, individuals with increased adherence to the type A and type B diets had greater reductions in BMI and waist circumference, respectively ($p < 0.01$) [6]. Furthermore, individuals with increased type O diet adherence showed decreased BMI and waist circumference ($p < 0.01$). On the other hand, it is interesting to investigate the bacterial associations with impaired lipid and glucose metabolism. The role of bacterial pathogens in glucose metabolism disturbances is confirmed by the arising facts of glucosyltransferases found in bacteria. Thus, the glycosyltransferase GT1 was isolated from *Bacillus cereus* [7].

Glycosyltransferases of bacterial origin can use a large diversity of donor and acceptor substrates, thus interfering with glucose levels [8, 9]. Diabetes mellitus might manifest clinically due to the interplay of bacterial glycosyltransferases that may use host sugar nucleotides as donors for glycosyl transfer to acceptors for structural purposes. The present study aimed to find the peculiarities of ABO blood group types in patients with hypercholesterinemia, hyperglycemia and pathology of connective tissue.

## MATERIALS AND METHODS

A case-control study was conducted from April 2019 to September 2021. All blood was drawn from patients into heparin Vacutainer tubes following informed consent. Serum cholesterol, glucose and usual biochemical parameters were measured by standard biochemical methods. In addition, a bacterial investigation of the synovial fluid was performed on 43 patients. Blood group type was defined by the direct method of agglutination using standard IgM monoclonal antibodies approved as reliable for use in clinical practice [10] anti-A and anti-B antibodies. In addition, 50 patients (26 with hypercholesterinemia and 24 with normal levels of serum lipids, 27 men and 23 women) aged 62.0 ± 2.1 years with gonarthrosis and coxarthrosis were analyzed for ABO frequency phenotype. The patients were also divided by the level of glucose (29 with high values and 21 with normal values). The patient group contained participants who had elevated glucose levels. In contrast, the control group included participants who had normal glucose levels. Information was collected through a self-administered questionnaire. Detection of IgM, IgG, IgA antibodies, autoimmune lymphocytotoxic and granulocytotoxic antibodies, and the reaction of leukocyte migration inhibition with tissue, bacterial and fungal antigens were performed for all patients. The mean ± SD of the parameters are presented. Statistical analysis was performed using the software Statistica 10.0.

## RESULTS

Patients with increased cholesterol levels showed increased erythrocyte sedimentation rate (ESR), levels of leukocytes, neutrophils, glycoproteins, total protein, sialic acids, creatinine, bilirubin, thymol probe, alkaline phosphatase, urea, chondroitin sulfates, CRP, calcium, autoimmune lymphocytotoxic antibodies, autoimmune granulocytotoxic antibodies, IgM, IgA, IgG antibodies, spontaneous leukocyte migration index (LMI), LMI to bone, fibrotic circle, LMI to *S. pyogenes* (Table 1).

In turn, patients with hypercholesterinemia showed lower hemoglobin levels, erythrocytes, young neutrophils, monocytes, eosinophils, LMI to pulposus nucleus, cartilago, *S. aureus*, *E. coli*, and *P. vulgaris*.

The values of systolic blood pressure appeared to be higher in persons with hypercholesterolemia (126.25 ± 1.37 mm Hg) as compared to the persons with normal levels of cholesterin (117.5 ± 1.2 mm Hg) as well as higher diastolic blood pressure (83.75 ± 1.1 mm Hg and 75.0 ± 1.0 mm Hg accordingly). In addition, patients with hypercholesterinemia, as compared to normal levels of cholesterol demonstrated higher values of alanine aminotransferase (ALT) (27.41 ± 1.3 units/l and 22.8 ± 1.0 units/l), aspartate aminotransferase (AST) (30.0 ± 1.5 units/l and 28.6 ± 1.4 units/l), circulating immune complexes (93.5 ± 2.4 and 87.25 ± 2.1 units).

Persons with the absorbing ability of anti-B IgG antibody showed higher cholesterol levels. Persons with A blood group type (40%) showed higher frequency in the group with hyperlipidemia as compared to O (40%) and B blood group types (20%). Less frequency of A blood group type (33%) was observed in the group with normal level of lipidemia as compared to O blood

***Table 1. Biochemical parameters according to the level of cholesterin in patients with pathology of connected tissue***

| | B lipoproteins < 50 mmol/l | B lipoproteins > 50 mmol/l |
|---|---|---|
| Leucocytes | 5.98 ± 0.61 | 6.64 ± 0.70 |
| Neurophils | 52.6 ± 1.1 | 58.15 ± 1.3 |
| ESR | 9.8 ± 0.8 | 25.15 ± 0.92 |
| Glycoproteins | 0.54 ± 0.02 | 0.79 ± 0.02 |
| Proteins | 80.7 ± 21 | 77.0 ± 1.7 |
| Bilirubin | 5.6 ± 0.04 | 19.6 ± 0.1 |
| Alkaline phosphatase | 1.5 ± 0.01 | 6.8 ± 0.04 |
| Ca | 2.35 ± 0.02 | 2.52 ± 0.02 |
| Sialic acids | 120 ± 71 | 222.5 ± 84 |
| Urea | 3.0 ± 0.3 | 4.5 ± 0.31 |
| Creatinine | 77.0 ± 1.3 | 82.5 ± 1.4 |
| Chondrotin sulfates | 0.078 ± 0.01 | 0.311 ± 0.04 |
| Authoimmune lymphocytotoxic antibodies | 7.0 ± 0.1 | 11.2 ± 0.03 |
| Authoimmune granulocytotoxic antibodies | 90.0 ± 0.2 | 9.75 ± 0.21 |
| Spontaneous LMI | 0.75 ± 0.01 | 1.32 ± 0.01 |
| LMI to bone | 1.15 ± 0.01 | 0.98 ± 0.01 |
| LMI to Str. Pyogenes | 1.0 ± 0.04 | 0.9 ± 0.01 |
| Thymole probe | 3.14 ± 0.3 | 4.3 ± 0.34 |
| ALT | 22.8 ± 0.74 | 27.41 ± 1.3 |
| AST | 28.6 ± 1.3 | 30.0 ± 1.34 |
| CRP | 31.5 ± 1.4 | 48.0 ± 1.52 |
| IgG | 13.6 ± 1.64 | 12.8 ± 0.5 |
| IgM | 1.28 ± 0.1 | 1.75 ± 0.14 |
| IgA | 2.33 ± 0.27 | 2.65 ± 0.31 |
| | | |
| Hemoglobin | 111.4 ± 1.7 | 128.5 ± 1.74 |
| Erythrocytes | 3.75 ± 0.22 | 4.22 ± 0.24 |
| Young netrophils | 3.0 ± 0.17 | 3.5 ± 0.18 |
| Monocytes | 5.6 ± 0.04 | 6.6 ± 0.05 |
| Eosinophils | 4.25 ± 0.03 | 2.0 ± 0.02 |
| LMI to *St. aureus* | 0.9 ± 0.01 | 0.84 ± 0.01 |
| LMI to pulposus nucleus | 1.08 ± 0.01 | 0.89 ± 0.01 |
| LMI to *E.coli* | 0.99 ± 0.01 | 0.67 ± 0.01 |
| LMI to *Pr. vulgaris* | 1.12 ± 0.01 | 0.9 ± 0.01 |
| LMI to cartilago | 1.1 ± 0.01 | 1.0 ± 0.01 |

group type (44%) and B blood group type (22%) (Figure 1). Thus, persons with A blood group type showed susceptibility to hyperlipidemia.

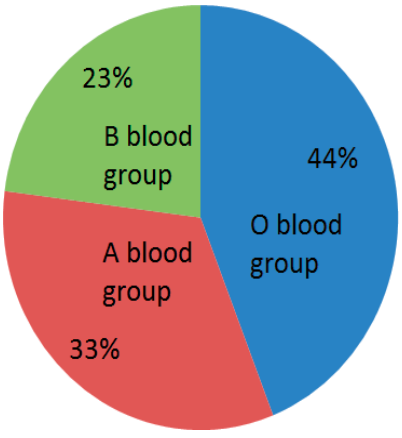


***Figure 1. The distribution of ABO blood group types among patients with normal levels of cholesterol***

The study revealed the predisposition of A (40%) and B (26.6%) blood group types to hyperglycemia. In contrast, the O blood group has been detected in fewer cases (33.3%).

A higher percentage of persons with B blood group type (32%) and A blood group type (40%) showed increased glucose levels. On the other hand, the O blood group type appeared to be of the highest frequency among people with normal glucose levels.

Persons with hyperglycemia showed increased levels of hemoglobin, erythrocytes, ESR, lymphocytes, proteins, thymol probe, alkaline phosphatase, acid phosphatase, calcium, phosphorus, and urea.

In turn, hyperglycemia has been associated with lower number of leukocytes, young neutrophils, segmented neutrophils, monocytes, and lower levels of CRP, glycoproteins, ALT, AST, and haptoglobin (Table 2). The study also revealed increased leukocyte migration activity to *St. aureus*, *Ps. aeruginosa* and *Esche-*

***Table 2. Biochemical parameters according to the level of glucose***

| | Glucose < 5.0 mmol/l | Glucose > 5.0 mmol/l |
|---|---|---|
| Hemoglobin | 118.6 ± 1.42 | 122.54 ± 1.7 |
| Erythrocytes | 4.0 ± 0.21 | 4.29 ± 0.24 |
| ESR | 22.94 ± 1.1 | 25.0 ± 1.3 |
| Lymphocytes | 26.72 ± 1.0 | 28.9 ± 1.2 |
| Proteins | 72.1 ± 1.4 | 78.73 ± 1.42 |
| Cholesterin | 4.06 ± 0.8 | 4.67 ± 0.84 |
| Thymol probe | 3.61 ± 0.01 | 4.45 ± 00.2 |
| β-lipoproteins | 43.72 ± 1.1 | 55.33 ± 1.4 |
| Alkaline phosphatase | 255.1 ± 3.2 | 280.94 ± 4.0 |
| Acid phosphatase | 2.9 ± 0.04 | 3.55 ± 0.05 |
| Ca | 2.23 ± 0.04 | 2.31 ± 0.05 |
| P | 1.36 ± 0.02 | 1.62 ± 0.03 |
| Urea | 4.55 ± 0.04 | 4.98 ± 0.05 |
| | | |
| Leukocytes | 7.69 ± 0.8 | 7.26 ± 0.84 |
| Young neutrophils | 4.1 ± 0.01 | 3.83 ± 0.01 |
| Segmented neutrophils | 60.5 ± 1.2 | 58.9 ± 1.3 |
| Monocytes | 6.66 ± 1.1 | 6.0 ± 1.0 |
| CRP | 33.75 ± 1.24 | 6.45 ± 1.0 |
| Glycoproteins | 0.83 ± 0.01 | 0.8 ± 0.01 |
| ALT | 34.72 ± 1.2 | 26.83 ± 1.1 |
| AST | 34.27 ± 1.2 | 27.27 ± 1.0 |
| Haptoglobin | 1.5 ± 0.01 | 1.4 ± 0.01 |

*richia coli* in persons with hyperglycemia. In addition, persons with hyperglycemia demonstrated an appearance of *Candida lusitaniae, Staphylococcus hominis, Acinetobacter* and *Bacillus subtilis* in bacterial findings from wounds and increased frequency of *Staphylococcus aureus* (n = 10), *Staphylococcus intermedius* (n = 8) and different types of *Staphylococci*.

## DISCUSSION

ABO blood groups are inherited antigenic substances found on erythrocytes as well as other tissues. Certain studies advocated that the ABO blood group might be associated with atherosclerosis and diabetes mellitus. Therefore, the conducted study aimed to reveal the association between the ABO blood group with hypercholesterolemia and hyperglycemia.

A blood group appeared to be predisposed to obesity, which agrees with other studies [11, 12]. O blood group type occurred to be the least suspected of hypercholesterinemia.

AB blood group was shown to have the least risk for hyperlipidemia, whereas the A blood group has been reported to have the highest risk for atherosclerosis [11, 12], whereas the O blood group – the least [3].

Patients with hyperglycemia showed increased levels of hemoglobin, erythrocytes, ESR, lymphocytes, proteins, thymol probe, lipoproteins, alkaline phosphatase, acid phosphatase, calcium, phosphorus, and urea.

On the other hand, hyperglycemia was associated with lower numbers/levels of leukocytes, young neutrophils, segmented neutrophils, monocytes, CRP, glycoproteins, ALT, AST, and haptoglobin as compared to the persons with normal levels of glucose.

A and B blood group types were found to be more predisposed to hyperglycemia, that has been described by other researchers. Persons with the O blood group appeared to be of the highest frequency among the patients with normal glucose levels.

Specific hypothesis advocates that genetic predisposition like “ABO” blood group would be associated with the occurrence of diseases including type 2 diabetes. Blood group “B” was associated with a high incidence of type 2 diabetes, and blood group “O” has a minimum association with type 2 diabetes [13]. Other researchers found that those with either the A or B blood group were at increased risk of type 2 diabetes mellitus compared with those with the O group. The authors suggested that people with the O blood type have a lower risk of developing type 2 diabetes mellitus characterized by insulin resistance and declining islet B-cell function, eventually leading to islet B-cell function failure [14].

The study by Pakistan researchers found a significant association between blood group B and type 2 diabetes mellitus (p = 0.006), whereas a negative association was seen between the blood group O and type 2 diabetes mellitus (p = 0.001) [15]. Geographical differences in the associations of diabetes mellitus with ABO phenotype have inspired us to conduct our study.

The conducted study revealed new associations of impaired glucose metabolism with immune sensitivity to bacterial and fungal pathogens. Persons with hyperlipidemia demonstrated leukocyte migration inhibition to *E. coli, P. vulgaris, S. aureus*, and *S. pyogenes*. In persons with hyperlipidemia, an appearance of *P. aeruginosa* and *C. lusitaniae* growth, various types of *Staphylococci*, as well as increased frequency of *St. aureus, B. subtilis*, Acinetobacter and increased growth of *E. coli* have been found. Patients with hyperglycemia demonstrated a high frequency of leukocyte migration enhancement to *S. pyogenes, P. aeruginosa, E. coli*, and *S. aureus*. In addition, persons with hyperglycemia demonstrated an appearance of *C. lusitaniae, S. hominis, Acinetobacter spp.*, and *B. subtilis* during bacterial growth from wounds, as well as increased frequency of *S. Aureus* and different types of *Staphylococci*.

A blood type has been reported to have a link with increased incidence of smallpox and *Pseudomonas aeruginosa* infection, B blood type – with increased incidence of gonorrhea, tuberculosis, *Streptococcus pneumoniae*, *E. coli* and salmonella infections, AB blood type – with increased incidence of smallpox, *E. coli* and salmonella infections [1].

Diabetes mellitus, hypercholesterolemia, arterial hypertension, and family history of ischemic heart disease are the most common risk factors for cardiovascular diseases and can be genetically transmitted to offspring. The link between the ABO blood type and thromboembolic diseases and bleeding risk is intervened by the glycosyltransferase activity, plasma levels, and biologic activity of vWF (Von Willebrand factor), a carrier protein for coagulation factor VIII, which is low in O type [1].

Glucose intolerance has been reported in persons with infection caused by *E. coli*. In addition, hyperglycemia has been associated with aggressive infectious diseases caused by *Streptococcus* [16], *Candida species* [17], and *Pseudomonas aeruginosa* [18].

The role of microbiota is considered to be decisive in different pathology, including infertility [19]. B antigen blood group activity was observed in Gram-negative bacteria, such as *E. coli* and *P. aeruginosa* [20, 21]. *E. coli* and *P. aeruginosa* infections were associated with increased serum triglycerides [22]. Thus, interactions of Gram-negative infection with the development of glucose intolerance might be the prospective trend for the immunological studies.

The clinical significance of the findings of ABO blood group type associations with hyperglycemia and hypercholesterolemia allows us to suggest that the ABO blood group represents a risk factor in subjects with coxarthrosis and gonarthrosis that can be used to further stratify risk for diabetes mellitus and atherosclerosis in this population of patients.

## CONCLUSIONS

A blood group was found to be predisposed to obesity, whereas the O blood group type appeared to be the least suspected of hypercholesterinemia. A and B blood group types have been shown to be predisposed to hyperglycemia. Hypercholesterinemia was associated with leukocyte migration inhibition to *Escherichia coli* and *Proteus vulgaris*, whereas hyperglycosemia – with leukocyte migration enhancement to *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Streptococcus pyogenes*. Knowledge of ABO blood groups might be useful for more personalized approaches toward health maintenance and the prevention of diseases.

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