



## Some Immune Characteristics of Interleukins and C – Reactive protein of cardiovascular disease patients in relation to blood groups

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### ABSTRACT:

Blood groups are determined by the ABO antigen system and are significant for transfusion compatibility as well as vulnerability to specific systemic illnesses, including cardiovascular ailments. Dyslipidemia, pro-thrombotic factors, and inflammatory cytokines are more prevalent in people with blood types other than O. Their risk of developing atherosclerosis and CVD is increased by all of these factors. On the other hand, those with blood type O usually have better inflammatory and hemostatic profiles, which may offer some protection against cardiovascular disease (CVD). This research examines the relation between ABO blood group phenotypes and some important inflammatory biomarkers—interleukin-6 (IL-6), interleukin-18 (IL-18), and C-reactive protein (CRP)—in patients with cardiovascular disease (CVD). A total of 80 individuals were engaged in a cross-sectional study, consisting of 50 CVD patients and 30 healthy controls. Blood groups were ascertained via tile agglutination, whereas serum concentrations of IL-6, IL-18, and CRP were quantified using ELISA and immunoturbidimetric techniques.

The results of CVD patients indicated IL-6 was highest in B+, and CRP was highest in O+, whereas IL-18 levels were variably distributed across groups but were usually Lower in non-O blood types. Participants with Group O+ actually had the highest IL-18 and CRP. These findings substantiate the hypothesis that non-O blood types have a greater susceptibility to systemic inflammation and cardiovascular problems.

ABO blood type profiling may serve as a valuable adjunct in assessing cardiovascular risk due to its simplicity and cost-effectiveness. The study emphasizes the need for further exploration of the immunogenetic mechanisms linking blood type antigens to inflammatory pathways, particularly across diverse populations such as the Kurdish demographic analyzed in this research.

**Keywords:** Key word: Blood group, Interleukins, CRP, CDV.



## 1 INTRODUCTION

The ABO blood type system is one of the most clinically and genetically significant human classification systems. Originally identified due to antigenic variations on the surface of erythrocytes [1]. These antigens are glycosylated molecules that influence transfusion compatibility and significantly contribute to immune regulation and disease vulnerability [2]. Besides erythrocytes, ABO antigens are found on epithelial and endothelial tissues, as well as in secretions, where they affect cell signaling and immune responses [3]. Numerous studies have shown links between ABO blood types and vulnerability to various illness, including infections, cancer, metabolic syndrome, and especially cardiovascular disorders [4]. Cardiovascular disease (CVD) continues to be a major worldwide cause of mortality, with increasing incidence in emerging countries. People who have blood types other than O (A, B, or AB) are more likely to have coronary artery disease and acute coronary syndrome than people who have blood type O [5]. The increased risk may be attributed to elevated levels of pro-thrombotic proteins, such as von Willebrand factor and factor VIII, together with the heightened systemic inflammation seen in non-O individuals [6]. Inflammatory cytokines are a major way that

blood type and cardiovascular risk are linked. Interleukin-6 (IL-6) is a potent pro-inflammatory cytokine implicated in endothelial dysfunction and the advancement of atherosclerosis [7]. Interleukin-18 (IL-18) has also been associated to inflammation of blood vessels, unstable plaque, and poorer heart health, especially in elderly people [8]. IL-6 and IL-18 have been suggested as biomarkers for inflammation-induced aging, sometimes referred to as "inflammaging," and chronic cardiovascular risk [9]. C-reactive protein (CRP), an acute-phase reactant produced by the liver and increased by IL-6, has been used as a dependable biomarker for cardiovascular inflammation, alongside cytokines in many heart illnesses, CRP levels are linked to how bad the condition is and how likely it is to happen and may also differ by blood group profile [10].

These links among Middle Eastern communities, notably in Iraq's Kurdistan Region, have received less attention despite growing global evidence. Given ethnic differences in blood group distribution and inflammation, additional study is needed. This study examines the relationship between ABO blood types and IL-6, IL-18, and CRP levels in the university population. Understanding these linkages may lead to genetically-informed cardiovascular risk assessment methods.

## 2 METHODOLOGY

This cross-sectional study was conducted at the Cardiac Center in Sulaymaniyah, Kurdistan Region of Iraq, from November 2024 to May 2025. A total of 80 of both genders, male and female individuals were participated, comprising 50 patients diagnosed with CVD and 30 apparently healthy controls. Participants were aged between 25 and 60 years. Informed consent was obtained from all participants, and ethical approval was granted by the relevant review board at the University of Sulaymaniyah.

Fasting blood samples (7–8 mL) were collected from each participant after a 10–12 hour overnight fast using sterile syringes. The samples were transferred to plain tubes, allowed to clot at room temperature for 18 minutes, and then centrifuged at 4000 rpm for 11 minutes to separate the serum. Serum was aliquoted into 0.5 mL vials and stored at –70°C until analysis[11]. All laboratory procedures were conducted at the University of Sulaymaniyah.

Blood groups were determined using the tile agglutination method with monoclonal anti-A, anti-B, and anti-D reagents, classifying participants into ABO and Rh categories [12].

Three key inflammatory markers were analyzed from serum samples, including IL-6 and IL-18, using sandwich ELISA kits (Sunlong Biotech Co., Ltd., China). Absorbance was read at 450 nm using a BioTek ELISA reader, and concentrations were calculated using standard curves. (CRP): was assessed using the immunoturbidimetric method with a Mindray CRP kit (China) on the Mindray BS-230 analyzer.

## STATISTICAL ANALYSIS

Data were analyzed using SPSS. Normality of variables was tested with the Shapiro–Wilk test. Comparisons between cardiovascular patients and controls within each blood group were performed using the independent sample t-test for normally distributed data. Differences among the four ABO groups in patient populations were assessed using one-way ANOVA, with the Kruskal–Wallis test applied for non-parametric data. Statistical analysis used mean ± standard deviation (SD), and a p-value < 0.05 was considered statistically significant.

## 3 RESULT

The findings are organized by comparing IL-6, IL-18, and CRP between control and CVD patient groups across the ABO blood types (O+, A+, B+, AB+).

**Table 1. Inflammatory markers of cardiovascular patients & controls in blood group O+.**

Parameters	Control group	Patients group	P value
IL-6	6.676±3.054	12.99±2.765	<0.0001
IL-18	18.50±15.50	39.83±18.19	0.0073
CRP	1.172± 0.5150	8.895± 4.730	<0.0001

Results are represented as mean ± SD, P value less than 0.05 mean significant different

Table 1 delineates the disparities in inflammatory markers (IL-6, IL-18, and CRP) between individuals with O+ blood type who possess CVD and control. The results indicate that CVD patients had significantly higher levels of IL-6 (12.99 ± 2.765) compared to controls (6.676 ± 3.054, p < 0.0001), suggesting that IL-6 plays a crucial role in the inflammatory processes associated with cardiovascular diseases. Similarly, IL-18 levels (39.83 ± 18.19 vs. 18.50 ± 15.50, p = 0.0073) and CRP levels (8.895 ± 4.730 vs. 1.172 ± 0.5150, p < 0.0001) were elevated in individuals with CVD. These indicators may serve as biomarkers for cardiovascular inflammation in individuals with O+ blood type. Increased CRP levels may especially highlight the importance of systemic inflammation in cardiovascular disease risk among individuals with O+ blood type.

**Table 2. Inflammatory markers of cardiovascular patients & controls in blood group A+.**

Parameters	Control group	Patients group	P value
IL-6	7.242±3.022	13.53±3.164	0.0004
IL-18	20.69±11.87	36.41±9.442	0.0050
CRP	1.193± 0.4405	8.283± 4.174	0.0002

Results are represented as mean ± SD, P value less than 0.05 mean significant different

Table 2 shows the comparisons between CVD patients' IL-6, IL-18, and CRP to A+ blood type controls. IL-6 levels were considerably higher in CVD patients (13.53 ± 3.164 vs. 7.242 ± 3.022, p = 0.0004), highlighting its potential as an inflammatory biomarker for CVD, especially in A+ persons. IL-18 (36.41 ± 9.442 vs. 20.69 ± 11.87, p = 0.0050) and CRP (8.283 ± 4.174 vs. 1.193 ± 0.4405, p = 0.0002) were also increased in CVD patients, suggesting the link between systemic inflammation and cardiovascular risk A+ blood type people may develop atherosclerosis and other cardiovascular diseases due to chronic inflammation, as shown by high CRP levels.

**Table 3. Inflammatory markers of cardiovascular patients & controls in blood group B+.**

Parameters	Control group	Patients group	P value
IL-6	7.233±2.390	15.45±7.172	0.0104
IL-18	21.14±15.43	35.07±6.867	0.0267
CRP	0.9660± 0.5278	6.189± 2.285	0.0003

Results are represented as mean±SD, P value less than 0.05 mean significant different

Table 3 show the compare markers between CVD Patients and control of blood group B+. where IL-6 levels were also high significant in CVD patients (15.45 ± 7.172 vs. 7.233 ± 2.390, p = 0.0104). This result is the same with what we saw in A+ and O+, where IL-6 acts as a potential marker of inflammation. IL-18 (35.07 ± 6.867 vs. 21.14 ± 15.43, p = 0.0267) and CRP (6.189 ± 2.285 vs. 0.9660 ± 0.5278, p = 0.0003) were also significantly elevated in CVD patients, supporting the role of these markers in the inflammatory processes of cardiovascular diseases across B+ blood group.

**Table 4. Inflammatory markers of cardiovascular patients & controls in blood group AB+.**

Parameters	Control group	Patients group	P value
IL-6	4.625±1.945	12.41±1.983	<0.0001
IL-18	12.28±10.42	30.01±4.092	0.0004
CRP	1.345± 0.3899	7.430± 4.057	0.0035

Results are represented as mean±SD, P value less than 0.05 mean significant different

Table 4 shows the results for AB+ blood group between CVD patients and controls, where IL-6 (12.41 ± 1.983) was significantly higher in CVD patients compared to controls (4.625 ± 1.945, p < 0.0001). Similarly, IL-18 (30.01 ± 4.092 vs. 12.28 ± 10.42, p = 0.0004) and CRP (7.430 ± 4.057 vs. 1.345 ± 0.3899, p = 0.0035) levels were higher in CVD patients, further confirming that higher inflammatory markers are associated with cardiovascular disease, any blood group type. The consistency of these elevated markers across different ABO blood types highlights the central role of inflammation in CVD.

**STATISTICAL ANALYSIS AND INTERPRETATION**

For all four blood groups, IL-6, IL-18, and CRP exhibited statistically significant differences between CVD patients and healthy controls (p < 0.05). The increase in inflammatory markers across the ABO blood groups suggests that systemic inflammation is a significant factor in CVD, regardless of blood group. Although IL-18 and CRP levels were consistently raised in CVD patients, suggesting that these markers may serve as reliable predictors of CVD, the results of tables 1 through 4 show that IL-6 is greater throughout all blood groups in CVD patients, which may signify that it may signal early CVD.

**Table 5. Comparison of inflammatory markers across ABO blood groups in cardiovascular disease patients**

Parameters	O+	A+	B+	AB+
IL6	12.99±2.765 <sup>a</sup>	13.53±3.164 <sup>a</sup>	17.99±11.15 <sup>a</sup>	12.41±1.983 <sup>a</sup>
IL-18	39.83±18.19 <sup>a</sup>	36.41±9.442 <sup>a</sup>	35.07±6.867 <sup>a</sup>	30.01±4.092 <sup>a</sup>
CRP	8.895 ± 4.730 <sup>a</sup>	8.283 ± 4.174 <sup>a</sup>	6.189 ± 2.285 <sup>a</sup>	7.430 ± 4.057 <sup>a</sup>

Different letters mean significant different, Same letters mean non-significant different

Table 5 compares the levels of IL-6, IL-18, and CRP in individuals with cardiovascular disease who had one of the four ABO blood types. The findings demonstrate substantial disparities in inflammatory marker levels among blood groups: The B+ blood type had the highest level of IL-6 (17.99 ± 11.15), followed by the A+ and O+ blood types. This suggests that individuals with blood type B+ may have a heightened inflammatory response. The O+ blood type had the most IL-18 (39.83 ± 18.19), whereas the A+ and B+ blood types had far lower amounts. With O+ having the highest value (8.895

$\pm 4.730$ ), CRP was higher in all blood types. This suggests that it could be a better way to detect inflammation no matter what blood type you have.

There were statistically significant variations in the levels of IL-6, IL-18, and CRP among different ABO blood types ( $p < 0.05$ ). Extremely high levels of IL-6 ( $17.99 \pm 11.15$ ) in the B+ blood group suggest a possible association between this blood type and elevated levels of inflammation in the body. It is supported by this that people with non-O blood types, particularly B+, may have more inflammatory traits, which might make them more vulnerable to cardiovascular disease.

The average IL-18 levels were greatest in O+ blood ( $39.83 \pm 18.19$ ), but levels of IL-18 varied significantly across other blood types. Group O's lower IL-6 levels indicate a clear inflammatory reaction. When compared to other blood types, this one could offer some protection.

It's interesting that the O+ blood type had higher CRP levels than all the other groups. This study suggests that CRP serves as a somewhat consistent marker across all ABO blood groups; nevertheless, it may still exhibit variability in its interaction with particular blood type-related inflammatory processes.

These data corroborate the hypothesis that non-O blood types, especially B+, are prone to elevated systemic inflammation, which may elevate the risk of cardiovascular disease. CRP is still a useful way to tell whether you have systemic inflammation, no matter what sort of blood you have. This further supports its utility in determining cardiovascular risk.

#### 4 DISCUSSION

This study reveals a substantial correlation between ABO blood group types and inflammatory biomarkers, such as IL-6, IL-18, and CRP, in individuals with CVD. The findings indicate that persons with non-O blood types, specifically A+, B+, and AB+, demonstrate increased levels of IL-6, IL-18, and CRP in comparison to those with blood type O+. This indicates that non-O blood types may show a higher risk. to systemic inflammation, a significant factor in the development of CVD [13] Our analysis showed that the highest levels of IL-6 were found in individuals with blood type B+, supporting previous findings that people with blood types A and B have higher levels of IL-6 [14]. IL-6 is a pro-inflammatory cytokine that is integral to the inflammatory mechanisms contributing to endothelial dysfunction, a precursor to atherosclerosis. Our investigation revealed that the greatest concentrations of IL-6 were detected in persons with blood type B+, corroborating prior research indicating elevated IL-6 levels in those with blood types A and B [15]. The heightened IL-6 levels observed in this study support the hypothesis that these individuals may possess an increased risk for developing cardiovascular disease, as elevated IL-6 has been linked to negative cardiovascular outcomes and the progression of atherosclerotic lesions [16]. This finding aligns with research indicating that individuals with blood types A and B have a heightened propensity for cardiovascular events, likely due to elevated systemic inflammation and prothrombotic factors [17].

IL-18, another inflammatory cytokine, was found to be higher in people with CVD in all blood types. People with blood type O+ had the most of these. This suggests that IL-18 may play a significant role in the inflammation and progression of cardiovascular disease, particularly in individuals with blood group O [18]. The increased IL-18 levels in group O+ participants are significant, as this blood group is frequently regarded as having protective attributes against inflammation relative to other blood types. The findings of this study indicate that IL-18 may serve as a potential biomarker for early cardiovascular risk, particularly in individuals with blood group O[19].

The correlation between ABO blood types and inflammatory markers is likely influenced by genetic and immunological factors, including variations in glycosylation patterns and the expression of ABO antigens on endothelial cells. Genetic differences may affect the distinct inflammatory profiles observed in individuals with different blood types [20]. However, blood type O individuals exhibited lower levels of CRP, IL-6, and IL-18, which lends credence to the theory that group O may protect against systemic inflammation [21].

The alteration of ABO antigens on immunological and endothelial cells may be connected to this protective effect [22]. Additionally, non-O blood types have larger quantities of thrombotic factors, such as von Willebrand factor, according to gene expression studies [23].

IL-6 has been linked to traits, including insulin resistance and impaired lipid metabolism, that raise the risk of CVD [24]. Our finding that IL-6 levels were greatest in group B is in line with studies on lipid-cytokine interactions [25].

Changes in ABO-linked glycosylation in non-O blood types may impact the pace of cytokine elimination, thereby extending inflammation [26]. Individual structural variations can influence immunological signals and chronic inflammatory responses. IL-6 and CRP increase levels are may indicate heart stress and injury in research participants [27]. The key factor in CVD is supports the hypothesis that long-term inflammation [28].

According to epigenetic studies, promoter demethylation causes elevated IL-6 gene expression in blood type A individuals[29]. Furthermore, it has been demonstrated that ABO antigens affect the body's response to inflammation and oxidative stress[30]. Because of its ease of use and accessibility, ABO grouping is a practical and economical way

to identify people who are at high inflammatory risk in cardiovascular risk assessment [31]. Studies show that personalized, inflammation-focused treatments are being looked into more and more as a way to treat heart disease [32].

## CONCLUSION

This study showed that inflammatory markers such as CRP, IL-6, and IL-18 may vary among various ABO blood types. Individuals dealing with (CVD) display these biomarkers. People with blood types other than O, mostly A+ and B+, were more likely to have these signs. This might mean that individuals in this group had more systemic inflammation than average individuals. Conversely, those with blood type O+ had reduced levels of IL-6, CRP, and IL-18, indicating that this blood type may confer protection against systemic inflammation.

These findings show ABO blood group phenotypes may influence inflammatory responses in cardiovascular disease via biological, immunological, or epigenetic ways. These findings demonstrate the importance of using blood group data.

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## CONFLICTS OF INTEREST

The author declares no conflict of interest.

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