
RESEARCH ARTICLE

Study of the Relationship between the NLRP3 and White Blood Cell to Determine Inflammation in Cardiovascular Patients

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ABSTRACT

The primary reason for mortality globally, cardiovascular conditions are particularly common across industrialised as well as disadvantaged to intermediate-income countries. A variety of risk factors, including inheritance, cigarettes, being overweight, lack of movement, and high blood pressure, had been discovered. Metabolic disorders and glucose intolerance are additional variables linked to heart disease. The Fifty specimens of blood used in the present investigation had been divided between twenty samples representing the control population as well as forty specimens among those suffering from heart failure. Hemoglobin, platelets, all white blood cell, as well as NLRP3 levels were measured within the current investigation among the untreated controls as well as individuals having cardiovascular illnesses. The present research discovered a relationship amongst NLR 3 and neutrophil, lymphocyte , and age. According the findings of the present research, individuals with cardiovascular disorders had significantly higher levels of platelets, whole white blood cells, and NLRP3 ($p < 0.05$) and significantly lower levels of haemoglobin ($p < 0.05$) than the unaffected group. Additionally, NLRP3 has been shown to positively correlate experiencing ages, the neutrophils, and especially lymphocytes in individuals with cardiovascular conditions. According to the present investigation, those suffering from heart failure had higher levels of inflammation-associated mediators, which may serve as a warning indicator for CVD.

KEYWORDS

NLRP3, CVD, WBC, Cardiovascular Patients.

ARTICLE INFORMATION

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1. Introduction

Arterial is one of the most common fundamental explanation for cardiac illnesses, which are diverse conditions involving abnormalities the heart as well as blood circulation (Kralj and Brkić Biloš, 2013). Although they progress progressively over the course of a person's life and remain absent from symptoms for a considerable amount of time, heart problems are regarded as persistent illnesses (Gaziano, 2001). Cardiovascular disorders have existed as among the leading causes of premature mortality worldwide for a long time. According to research, heart disease will claim the lives of 23.6 million people annually by 2030 (Kralj and Brkić Biloš, 2013).

Cardiovascular disorders are caused by a variety of variables, including some of them are fixed (genetic, age, gender), whereas certain others are changeable and subject to influence (physical, smoking, lipid disorders, diabetes, especially type 2 diabetes, hypertensive) (Reiner *et al.*, 2011). Controlling factors associated with risk (45–75%) and providing adequate medications for heart failure (25–55%) are the key to lowering the death rate due cardiac illnesses in relatively wealthy countries (Nascimento *et al.*, 2015). Considering the biggest reason of fatalities for Asians, Cardiovascular is a major health concern in Asian society (Ohira and Iso, 2013).

The occurrence of inflammation-related disorders like atherosclerosis, leading to structural as well as functional weaknesses of the arterial walls, is frequently linked to chronic inflammation. Inflammation brought on by hereditary and environmental factors causes atherosclerosis, which in turn causes vascular cell malfunction, causing coagulant obstruction. The main predictors during the appearance of coronary artery disease a condition typified by fatty acids accumulation, leukocytes penetration, and proliferated smooth muscle cells in the blood vessels structures, include increased the cholesterol and LDL cholesterol (LDL-C) quantities (Ference *et al.*, 2017). (Hansson, 2005). The physical The organism's initial level of protection was natural immunity, particularly triggered by known pathogens through systems known as pattern- recognizing receptors (PRRs). Natural immune system cells, including macrophages, neutrophils, and other cells associated with inflammation, have such receptors (Karasawa and Takahashi, 2017).

Within the cells structures called inflammatory proteins, which are part of the immune system that is born, cleave procaspase-1 to start pyroptosis and transform proIL-1 β as well as proIL-18 into matured versions. NLRP3 is an especially widely recognized inflammatory. The NLRP3, an inflammasome, IL-1 β , IL-18, and pyroptosis have all been demonstrated in multiple investigations to participate in a significant and significant impact on atherosclerotic. According to contemporary theories, cardiovascular disease is an inflamed, lipid-based illness, along with the inflammasome called NLRP3 is being implicated in the connection among infection and lipid breakdown given that it is activated by crystalline cholesterol and oxidized low-density lipoprotein (oxLDL), two substances that are prevalent in plaques associated with atherosclerosis. Furthermore, lysosome rupture, endoplasmic reticulum (ER) stress, damaged mitochondria, and reactive stress—all of which are linked to inflammatory activation—have recently been recognized as significant events related to atherosclerosis (Hoseini *et al.*, 2017).

Inflammatory substances have been found linked to cardiovascular conditions and suggested as additional cardiovascular risk factors (Bullón *et al.*, 2017). The most recent study has examined the function of the NLR subfamily pyrin domain carrying Three polypeptide (NLRP3) inflammatory in cardiovascular diseases. Heart attack, a condition known as coronary artery disease, diabetes, persistent heart failure, as well as hypertensive all cause the inflammasome associated with NLRP3 to become overexpressed. Lately, NLRP3 and IL-1 β have also been suggested as novel cardiovascular condition indicators (Bullón *et al.*, 2017).

Aim Present study that examines the connection between age and the progression of heart conditions as well as shows the relevance of inflammation-related indicators in the identification of these conditions.

2. Material and Method

The city of Karbala Laboratory to supply Cardiovascular Diseases and Treatment from Iraq conducted this investigation. In addition to those in the regulating group, blood samples were taken from individuals with cardiovascular conditions. Thirty specimens compared to individuals who had heart disease and twenty specimens to the unaffected population made the total number of fifty specimens that were analyzed.

2.1 Blood samples collection

Five milliliters of sterile liquid have been employed to extract the blood specimens through the veins. This specimen has been stored in 2tubes with labels; the initial set of containers includes EDTA, the anticoagulant that keeps blood from coagulation so it can be utilized for biological studies. During the additional set of containers, which were hydrogel tubes devoid of coagulant bleeding, was utilized to prepare the bloodstream for subsequent biochemistry and marker analysis. After centrifuging the donated blood for ten minutes at the speed of 6000 rpm to allow it to clot, the blood product was separated and frozen at -80 oC until the laboratory examination underlying the purpose of the research could be completed.

Hemoglobin Estimation

The Blood Laboratories used Mythic 18 (RINGELISA N CO., Turkey) for performing hematological measurements using EDTA samples. The full blood count, or CBC, of EDTA-anticoagulated plasma was determined by this totally computerized hematologic instrument (Wasmuth, 2010).

2.2. Human Inflammasome protein 3 (NLRP3)

The company-specialized kit was provided by Elabscience, The field of biotechnology to measure the levels of human NLRP3 in serum.

2.3 Statistical Analysis

The SPS software was used for statistically examining the information (SPSS, Version 23). The test for significance has been employed to compare the averages and standard errors of the study participants and the untreated group. Although a correlation coefficients was computed to determine the relationship among indicators and parameters, a Pearson correlation and one-way ANOVA by LSD were utilized to compare all subdivision groups according to the parameters that were measured. The

version of the Microsoft Office 2016 Excel application was used to create the figures. A substantial $P < 0.05$ was used for statistical analysis of each of them.

3. Results

3.1. Hematological studies

3.1.1. Comparison the level of Hemoglobin in patients with cardiovascular diseases and control group

Furthermore illustrated in figure (1), the current study's findings showed that people having cardiovascular illnesses had significantly lower hemoglobin levels (12.91 ± 0.39) than the individuals in the control group (13.55 ± 0.20) ($p < 0.05$).

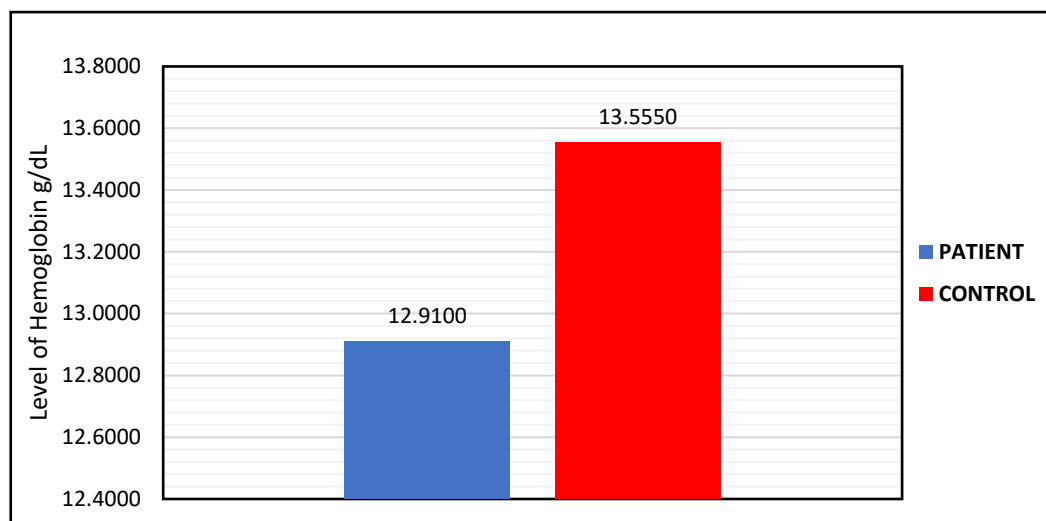


Figure 1: Comparison of Hb level between patients with cardiovascular diseases and control group

3.1.2 Comparison of the level of platelet in patients with cardiovascular diseases and control group

Furthermore, as seen in Figure (2), the present research's findings showed that individuals having cardiovascular disorders had a non-significantly higher ($p < 0.05$) platelet level (293.216 ± 13.883) than the unaffected group (282.8 ± 8.906).

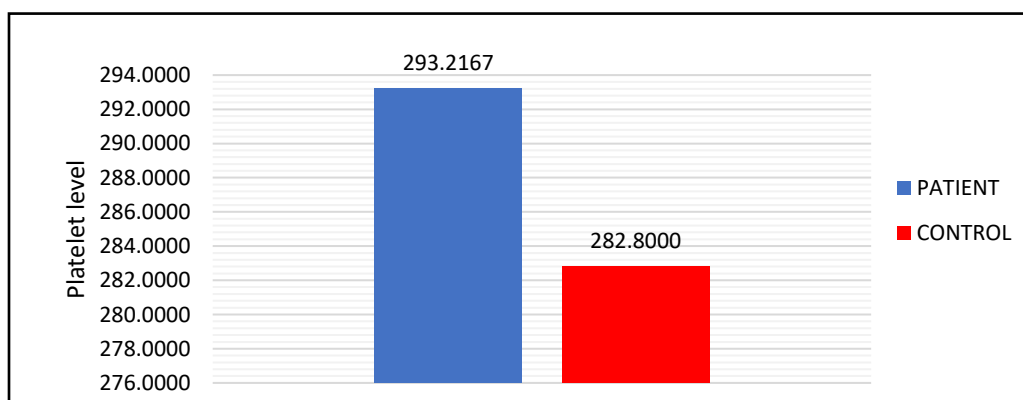


Figure 2: Comparison of platelets level between patients with cardiovascular diseases and control group

3.1.3. Comparison of the level of total white blood cells in patients with cardiovascular diseases and control group

Figure 3 shows that individuals with cardiovascular illnesses had a significantly higher concentration of total white blood cells (10.09 ± 0.84) than the unaffected category (6.17 ± 0.209) ($p < 0.05$).

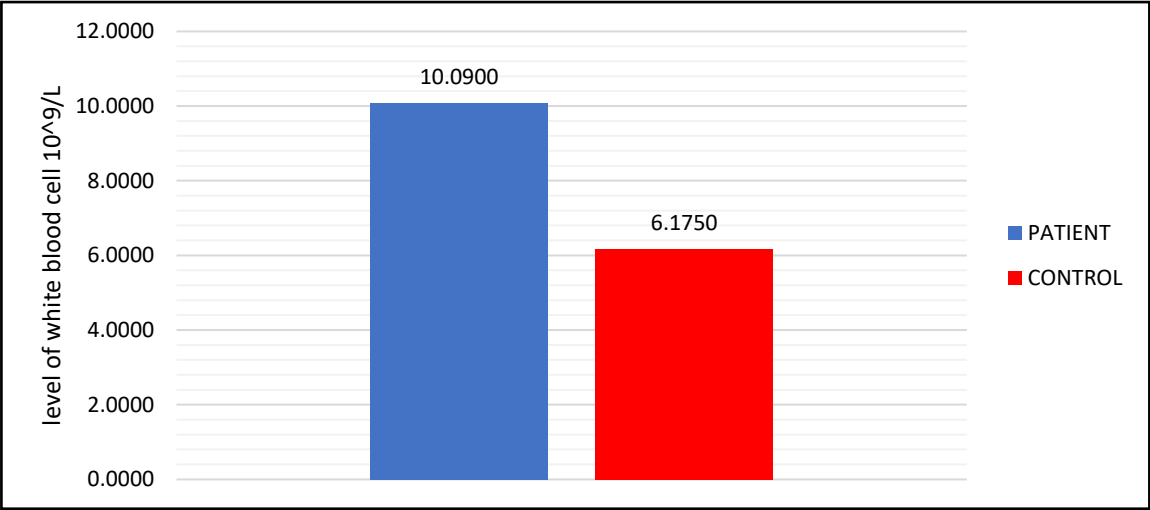


Figure 3: Comparison of white blood cell level between patients with cardiovascular diseases and control group

3.1.4. Comparison of the concentration of NLRP3 in patients with cardiovascular diseases and control group

NLRP3 levels in the categories under study are displayed in Figure (4-4). In contrast compared to the average of control groups (0.764 ± 0.054) ng/ml, the findings show a substantial ($p < 0.05$) rise in the mean concentration of NLRP3 in individuals having heart disease (1.096 ± 0.033) ng/ml.

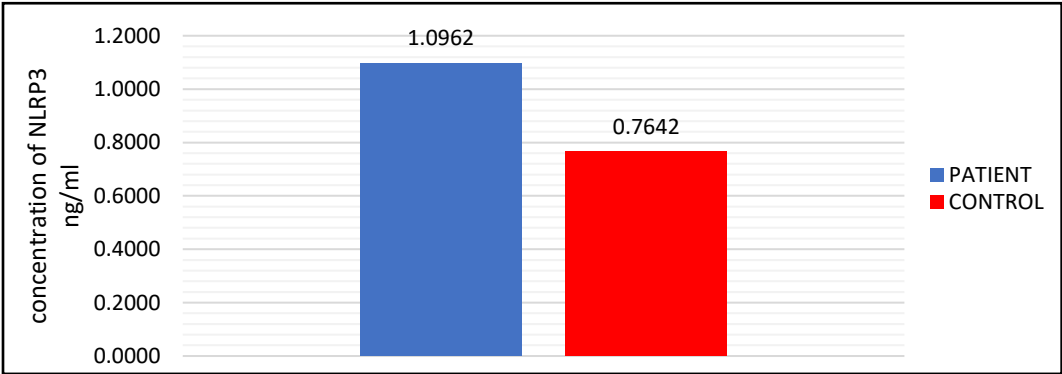


Figure 4: Comparison of NLRP3 concentration between patients with cardiovascular diseases and control group

3.2. Correlation between NLRP3 and Age

Figure 5 illustrates the findings from the relationship and linear regression study among NLRP3 concentration and ages for individuals experiencing cardiovascular illnesses, which showed a strong positive correlation ($r = 0.55$).

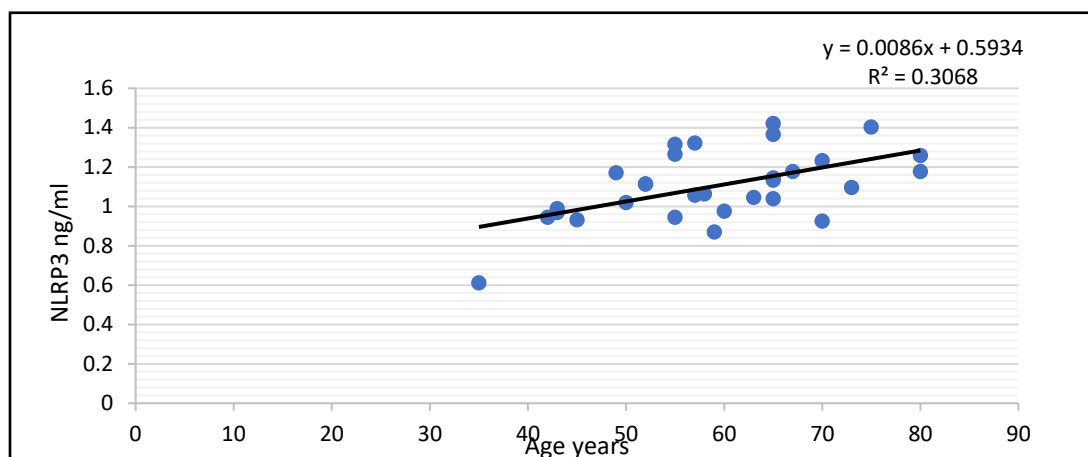


Figure 5: Correlation between the NLRP3 and age

3.3 Correlation between NLRP3 and lymphocytes

In individuals who had cardiovascular illnesses, the NLRP3 concentration and lymphocytes showed a substantial negative connection ($r=-0.5$), as shown in Figure (4-6).

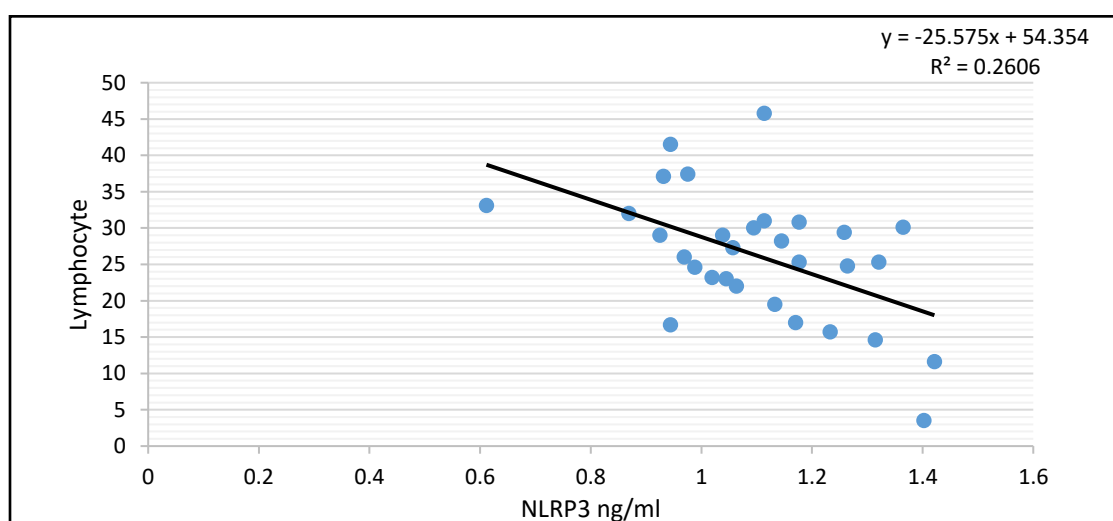


Figure 6: Correlation between the NLRP3 and lymphocyte

3.4 Correlation between NLRP3 and Neutrophils

In patients with cardiovascular illnesses, the NLRP3 concentration and lymphocytes showed a substantial positive connection ($r=0.46$), as shown in Figure (4-7).

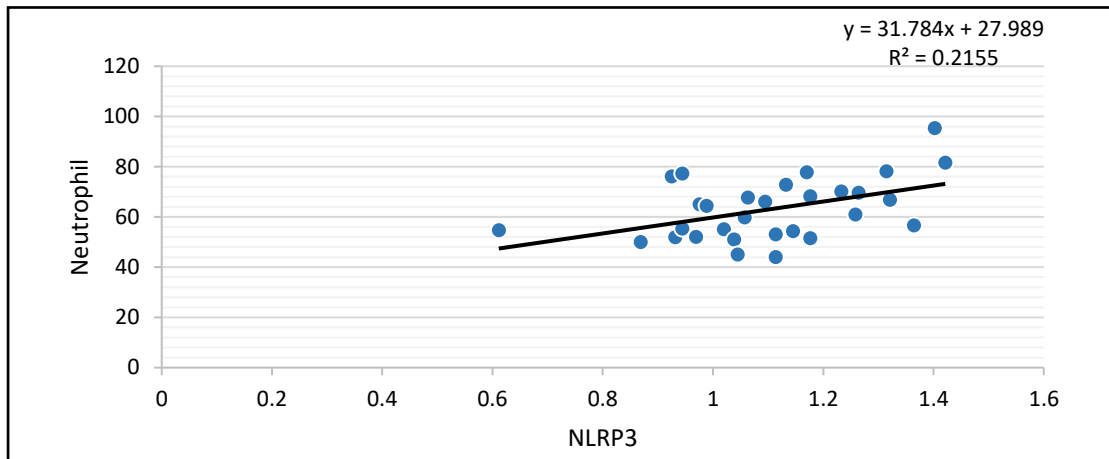


Figure 7: Correlation between the NLRP3 and Neutrophil

4. Discussion

The results of this research showed that individuals with cardiovascular illnesses had significantly lower hemoglobin levels ($p < 0.05$) than the untreated subgroup. This finding is consistent with research by Tul-Kubbra *et al.* (2020) that found that those with cardiac disease had lower hemoglobin levels than the control group. Reduced hemoglobin levels have been correlated to increased blood concentrations of fibronectin in males in good health (Coppola *et al.*, 2007), and anaemia has a role in the occurrence of myocardial ischemia and hypertrophy of the left ventricles (Bellotto and Cati, 2006). Furthermore, inflammatory cytokines with the value interleukin-1, interleukin-6, interferon- γ , and tumor necrotic factor α may cause moderate inflammation in order to raise the probability of CVD and reduced hemoglobin levels (Llauradó *et al.*, 2012).

The results of the present investigation showed that individuals having cardiovascular illnesses had non-significantly higher platelet levels ($p < 0.05$) than the untreated category. The findings, which are consistent with research by Siddig *et al.* (2020), suggest the numbers of platelets within the Cardiovascular category were significantly higher than those of the control group. The development of chronic thrombosis, including the advancement of atherosclerotic, is significantly influenced by elevated thrombi numbers and the stimulation of platelets. This condition may be caused by a shift in platelet counts in response to aberrant walls of the artery. Moreover, it has been shown that elevated platelet counts encourage inflammation and accelerate the progression of active atherosclerosis (Dong *et al.*, 2017). Furthermore, according to an investigation by Li *et al.* (2016), insufficiently activated platelets is a significant pathogenic component of coagulation during the location of blood vessel damage and causes CVD. Activation of platelets has also been significantly associated with platelet counts (Würtz *et al.*, 2012).

The average number of all white blood cells among individuals suffering heart failure was significantly higher ($p < 0.05$) than in the untreated group, according to the findings presented here. This conclusion is consistent with Tul-Kubbra *et al.* (2020), who determined that the test group (cardiac patients) had a considerably higher average white blood cell (WBC) count. Leukocytes are essential to the pathogenesis of cardiovascular disease, because many research investigations have shown that individuals with Atherosclerosis who have higher total leukocyte counts also have higher mortality rates (Grau *et al.*, 2004). One of the main characteristics of atherosclerotic is ongoing inflammatory processes, therefore the amount of white blood cells is a commonly used indicator of inflammatory in medical laboratories. Independent of the category, an elevated white blood cell count is linked to substantial plaque buildup in the coronary arteries on MDCT in asymptomatic patients alongside non-calcified lesions. White blood cell counts, particularly macrophage numbers, have been significant indicators of risk for Cardiovascular disease (CV) WBC may therefore, be an easily accessible and useful indicator of cardiovascular diseases in people who do not exhibit any symptoms (Kim *et al.*, 2017).

According to the data, people who suffered from cardiovascular conditions had a significantly higher average concentration of NLRP3 ($p < 0.05$) than those in the control and intervention categories. This work supports the findings of Niyonzimaa *et al.* (2020), who suggested a biological pathway linking CC-mediated inflammatory reaction in individuals associated pulmonary and coronary artery disease with both regional and systemically complementing and NLRP3 activation. Researchers demonstrate that complements play a role in the CC-driven inflammation that occurs isolated the atherosclerosis disease in individuals having CAD as well as in PBMC isolated individuals with ACS. Our findings suggest that the degree of severity and unpredictability of the illness are positively correlated with CC-induced complement and NLRP3 stimulation, whether systemically as well as underneath the atherosclerosis lesions.

Cardiac cells stimulation through the inflammasome linked to NLRP3 triggers immunological inflammation, including is essential for coronary artery disease ischemia/reperfusion (I/R) injury, and heart failure (HF) of various causes (Wang *et al.*, 2020). Within the research they conducted, Zheng *et al.* (2014) demonstrated that smokers with cardiovascular disease, diabetes, and high cholesterol had overexpressed NLRP3 in their aorta. Those participants' aortic NLRP3 transcription had an inverse relationship with HDL cholesterol levels and positively correlated with overall cholesterol level, LDL cholesterol level, particularly lipoprotein (a).

Within the cells structures called inflammatory cells can cleave pro-caspase-1 to start proptosis and transform pro-IL-1 β as well as proIL-18 into matured versions. One well-known inflammatory that plays a key part in atherosclerosis is NLRP3. Recently was recently demonstrated the inflammasome known as NLRP3 speeds up the developing of atherosclerosis by influencing a number of physiological and molecular targets, including reactive oxygen species, or PKR, the transcription factor JNK, STAT, MAPK, including the microRNA system. Inflammasome stimulation may be impacted through certain pathological conditions linked to coronary artery disease including as oxygen depletion, dysfunctional mitochondria, stress caused by the ER, and Lysosomes disruption. Determining the worth of these compounds as possible targets for treatment in atherosclerotic requires a deeper comprehension underlying physiology including the activation/inhibition processes performed by inflammatory cells (Hoseini *et al.*, 2017). A crucial step in a number of endothelium lesions involves the stimulation of an inflammasome called NLRP3 in ECs. Another among the main causes of atherosclerotic is the use of cigarettes. Cigarette stimulates NLRP3 and ASC communication, activates the NLRP3 the inflammasome, and causes pyroptosis in human aortic epithelial cells. (Wu *et al.*, 2018).

The NLRP3 and age percentages in individuals with cardiovascular diseases were shown to be significantly positively correlated ($p < 0.05$). This finding is consistent with a research investigation by Marín-Aguilar *et al.* (2020), which discovered that the main pathogenic mechanism associated with cardiovascular illnesses in individuals in good health is senescence. If characterized, the primary age-related alterations to the cardiovascular system's architecture as well as functioning during typical aging, might provide fresh insights into how to prevent ageing-specific cardiovascular dysfunction. The research has shown that by altering a number of aging-related characteristics, NLRP3 is linked to a longer lifespan and better health.

Little has been studied about the role of NLRP3 inhibition during aging, and nothing has been studied about longevity. Our data, such as glucose tolerance, are consistent with previous studies on the effect of NLRP3 ablation on aging (Youm *et al.*, 2013). Inflammation is highly associated with aging and age-related diseases and many rejuvenation strategies adopt anti-inflammatory diets (Finkel, 2015; Fontana *et al.*, 2012). Increased systemic inflammation is commonly concomitant with metabolic alterations and the deterioration of metabolic health, including the appearance of increased adiposity, insulin resistance, and dyslipidemia, which could prove to be a key determinant of a shortening lifespan and health span (Finkel, 2015).

In those suffering from cardiovascular conditions, the present research's findings indicated a substantial negative ($p < 0.05$) association between NLRP3 concentration and lymphocytes. It is consistent with the Siddig *et al.* (2020) investigation. The currently underway investigation showed that during comparison to healthy individuals, the amount of lymphocytes was considerably lower in those with cardiovascular disease. In individuals who have CAD and persistent coronary artery disease, a low blood lymphocyte count has been linked to poorer cardiovascular conditions. That is explained by the fact that enhanced lymphocyte death causes a drop in lymphocytes numbers in situations of chronic infection. The current data supports earlier research showing that individuals having Atherosclerosis experience decreased comparative overall quantitative lymphocyte percentages (Suzuki *et al.*, 2013). Cardiomyocyte engagement of the inflammasome known as NLRP3 triggers immunological inflammation and is essential for atherosclerosis, ischemia/reperfusion (I/R) injury, and heart failure (HF) of various causes (Wang *et al.*, 2020).

According to the present research's findings, individuals who have heart disease have a favorable link between their neutrophil count and NLRP3 percentage. According to an investigation by Tul-Kubbra *et al.* (2020), patients with cardiac disease had a considerably higher percentage neutrophil count, while those who were healthy had a lower % lymphocyte count. The regulatory role of neutrophils is linked to their extended retention in tissues as a result of reduced apoptotic and disrupted elimination through macrophages, as well as their increased recruitment from the bloodstream by defective endothelial (Rathod *et al.*, 2017). A crucial step in a number of endothelium lesions involves the activation of the inflammasome called NLRP3 in ECs. One of the main risk factors for atherosclerosis is smoking tobacco products. Depending to those investigations, which at first discovered an increased association between NLRP3 and neutrophils among individuals alongside cardiovascular conditions, nicotine increases the production of the two proteins NLRP3 and ASC and causes proptosis and inflammation caused by NLRP3 across humans. The aortic tissue cells (Wu *et al.*, 2018).

5. Conclusion

According to the results of the present research, people with cardiovascular conditions are carriers of the activated NLRP3 inflammasome, which plays an essential function in the formation of cardiovascular disorders and can be used as an early indicator of CVD. Even Nevertheless, the investigation discovered that elevated platelet counts in people with cardiovascular

disease may indicate a development in thrombosis. One of the suggestions made by the research is to examine the NLRP3 within a significant percentage of heart failure individuals. Examine the effects of NLRP3 on additional illnesses, including persistent kidney failure.

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