

# Association of Interleukin-17A with Biomarker Levels in Chronic Kidney Disease Patients

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## Abstract

Chronic kidney disease (CKD) considers as a progressive condition correlated with systemic inflammation, which pays to complications such as cardiovascular disease and renal dysfunction. However, Interleukin-17A (IL-17A), a pro-inflammatory cytokine, plays a serious role in immune regulation and inflammation. This research examines the association of serum IL-17A and biomarkers (creatinine, Beta 2 Macroglobulin) levels in patients with CKD. A case-control study was conducted involving 60 CKD patients and 30 healthy controls at Imam Al-Hussein Medical-City hospital in Kerbala, Iraq, from August to October 2024. Blood and urine samples were collected from all participants, and IL-17A were tested utilizing an ELISA kit. The results stated significantly higher serum IL-17A levels in patients with CKD ( $24.56 \pm 9.60$  pg/mL) compared to controls ( $5.65 \pm 1.84$  pg/mL),  $p = 0.0007$ . Moreover, levels of creatinine in CKD patients ( $0.96 \pm 0.51$  mg/dL) were significantly elevated compared to controls ( $0.27 \pm 0.10$  mg/dL),  $p = 0.0002$ . These findings stated that elevated IL-17A levels are associated with CKD and may pay to chronic inflammation, exacerbating renal damage. Furthermore, serum creatinine and Beta 2 Macroglobulin remnants a reliable biomarker for assessing kidney function. Increased IL-17A levels in CKD patients could serve as potential biomarkers for disease progression and targets for therapeutic interventions aimed at mitigating inflammation and improving patient outcomes.

**Keywords:** Interleukin 17A, Creatinine, CKD, Chronic Kidney Disease.

## 1. Introduction

Patients with CKD exhibit diverse levels of impaired kidney function and lowered glomerular filtration rate (GFR) [1], [2]. A uremic syndrome, which has been correlated with an extremely poor prognosis, is a defining characteristic of patients who advance to end-stage renal disease (ESRD). It is believed that CKD is thought to be a significant factor that can either cause or exacerbate a wide range of diseases, including cardiovascular diseases [3], [4], anemia [5], [6], electrolyte issues [7], [8], bone diseases [9], [10], cognitive and behavioral health issues, and an extensive variety of distinct diseases [11]. Nevertheless, it has been hypothesized that systemic inflammation plays a part in the development of atherosclerosis and can serve as a predictor of cardiovascular diseases in people who have CKD [12], [13]. There consistently exists a significant cause for anxiety when it deals with inflammation among those who receive treatment like hemodialysis [14]–[16]. Further, inflammatory signs and indicators have recently been identified in the sera of approximately between a third and half of patients with CKD or those undergoing dialysis, including C-reactive protein (CRP) [17]–[21].

Various immune cells, such as lymphocytes, have the ability of producing the proinflammatory cytokine IL-17 [22]–[25]. The binding of this cytokine to its numerous receptors has been demonstrated, which are made of a variety of isoforms, in a wide range of tissues across the body. In accordance to reports, people suffering from asthma, cancer and it has been proven that individuals with arthritis have elevated levels of IL-17 [26]. IL-TH17 lymphocytes are one of the plenty immune cells serve as significant process of IL-17. Furthermore, it has been noticed that IL-17 play a role in the autoimmune mechanisms associated with conditions including multiple sclerosis, rheumatoid arthritis, and diabetes [27]. IL-17, a form of chemokine, could possess an essential function in the recruitment of neutrophils to inflamed tissues, including the intestine, central nervous system, joints, and lungs [15]. On the contrary, research indicates that nearly 50% of patients receiving peritoneal dialysis may exhibit a proinflammatory state, as demonstrated by increased CRP ranges [15], [28]. Consequently, taking into account the role of inflammation in the progression of atherosclerosis, it is crucial to identify inflammatory factors along with treating the condition for those taking dialysis [3], [29]. The objective of this study is to evaluate the impact of the IL-17 and biomarkers parameters level such as creatinine, Beta 2 Macroglobulin in CKD patients.

## 2. Materials and Methods

The present research is a case-control investigation that was carried out on sixty patients who had been diagnosed with chronic kidney disease (CKD) and thirty healthy controls who were admitted to the Imam Al-Hussein Medical-City hospital in Kerbala, Iraq. The time period from August 2024 to October 2024 was utilized for the reason of carrying out this investigation. Examinations were performed on each and every patient prior to the medication had been started. We have requested that every patient who has chronic kidney disease bring someone they know or family member with them in order to make the procedure of obtaining controls considerably simpler. Furthermore, we were successful in obtaining additional controls from the same hospital that was used to enroll patients initially.

### 2.1 Inclusion and Exclusion Criteria

Patients of males and females, between the ages 20 to 70 years, residing in the province of Kerala, confirmed to have CKD by a nephrologist, and exhibiting a GFR of 30 to 89, had been included in the research study. Exclusion criteria included the diagnosis of other chronic diseases, along with people suffering from inflammatory and viral conditions. Particularly those with bowel disease, all type of hepatitis virus, psoriasis, rheumatoid arthritis, human immunodeficiency virus, lung infections, COVID-19, tonsillitis, and influenza had been excluded. [38].

### 2.2 Collection and handling of blood samples

In the week leading up to the blood withdrawal, the participants did not engage in any physical activity or take any analgesics. All of those enrolled were asked to refrain from consuming any food or beverages after 9 o'clock the night prior their blood was collected. Ten milliliters of blood has been extracted from antecubital artery after a fast that lasted between eight and ten hours overnight. Before using a disposable plastic syringe to puncture the vein, the nurses who were adequately trained provided every person with an explanation of the technique. This was done in order to provide the participants with a sense of understanding and confidence. In order to collect blood, three distinct kinds of tubes

have been used: yellow, purple, and blue. From 7 to 8 o'clock in the morning, all of the blood samples had been collected. After that, the blood samples were stored in a cool room for thirty minutes. After that, the samples have been isolated utilizing centrifugation from the cells at three thousand times the force of gravity for ten minutes. Snap-frozen plasma was kept at a temperature of -20 degrees Celsius until it was tested. Before processing, purple tubes was set with a blood lab equipment mixture. This was done in order to get values of glycohaemoglobin A1C, which was noted as hemoglobin total ratio. Every single sample was handled in the same manner in accordance with the standardised technique.

### **2.3 Collection and handling of urine samples**

Samples of urine have been obtained in sterile containers during the early morning prior to obtaining blood samples. Subsequently, within the same morning, an adequate urine sampling had been meticulously placed in a 6 ml sterilized standard vial, making use of a 50 ml disposable plastic syringe following the removal of the needle. The entire set of samples have been kept in a refrigerator until a sufficient quantity was gathered and examined in triplicate. All participants have been asked for providing a midstream, uninterrupted urine sample. A cartoon film was presented by a team member, tasked with detailing the step-by-step process of midstream urine collection. This initiative aims to assist all participants in accurately following the steps to obtain a midstream sample of urine that is both pure and typical.

### **2.4 Measuring of serum plasma interleukins**

An Enzyme-Linked Immunosorbent Assay (ELISA) kit was utilized in order to determine the amounts of IL-17 that had been detected in the plasma. My-bio-source, a firm based in the United States, delivered the ELISA kits, and an autoanalyzer was used to measure the blood creatinine levels of all of the patients who participated in the kidney function test. After measuring each sample three times, the overall average quantity for every observation was subsequently evaluated being prepared for data analysis following the completion of the measurements. All samples were evaluated without any dilution, and the procedure that was provided by the manufacturer of the assay was adhered very rigorously.

## **3. Data Analysis**

The statistical analysis was performed with IBM SPSS Statistics version 23. The results from the analysis were subsequently summarized using descriptive statistics. Likewise, the Mean and Standard Deviation have been determined. A probability criterion of  $p < 0.05$  was utilized to evaluate the statistical significance of the experimental results. Moreover, the Shapiro-Wilk test has been employed to determine the normality of the data. Additionally, the Independent T-Test was utilized to determine statistical differences between two distinct groups.

## **4. Results**

### **4.1 Interleukin -17 A**

This section states the results of the IL-17A in control and patients with CKD. However, there was a significant difference in IL-17A concentration levels between the control group and patients with CKD

as demonstrated in Figure 1. The reported mean of IL-17A is  $5.65 \pm 1.84$  pg/mL for control group, while there is markedly higher level at  $24.56 \pm 9.60$  pg/mL for patient with CKD. The result indicates that people who are suffering from chronic kidney disease have significantly elevated levels of IL-17A. The statistical analysis pointed out a p-value of 0.0007, which is considerably lower than the threshold of 0.05 that is typically accepted in the scientific field. The fact that this is the case implies there is a statistically significant difference in the concentrations of IL-17A across both of the groups. Regarding the findings, it is feasible that IL-17A contributes in inflammatory reactions that interact with CKD.

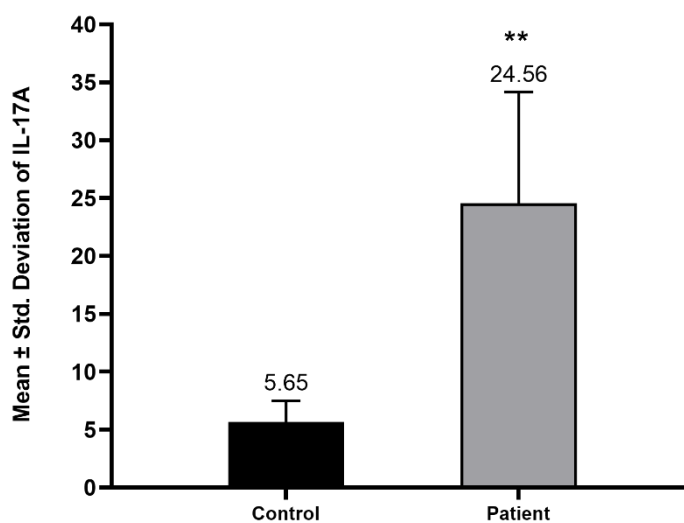


Fig. 1. The Comparison of serum IL17A Level within patients suffering CKD and their corresponding controls.

#### 4.2 Creatinine

The results that are observed, which are depicted in Figure 2, compare the concentrations of creatinine and beta-2 macroglobulin in patients who have chronic kidney disease (CKD) to those in a control group. There has been a significant difference in the levels of creatinine and beta-2 macroglobulin that were found between the two groups, as demonstrated by the results obtained. The control group shows an average creatinine level of  $0.27 \pm 0.10$  mg/dL, in comparison to patients with CKD demonstrate a significantly higher typical concentration of  $0.96 \pm 0.51$  mg/dL. The p-value for the result is 0.0002, which indicates that it is statistically significant. As an additional point of importance, the control group highlights an average Beta 2 Macroglobulin level of  $2.39 \pm 0.74$  mg/dL, whereas people who have chronic kidney disease had a considerably raised average level of  $6.32 \pm 2.19$  mg/dL within the same group. A p-value of 0.0001 indicates that this difference is statistically significant, revealing that there is a notable link between increasing levels of creatinine as well as Beta 2 Macroglobulin and CKD.

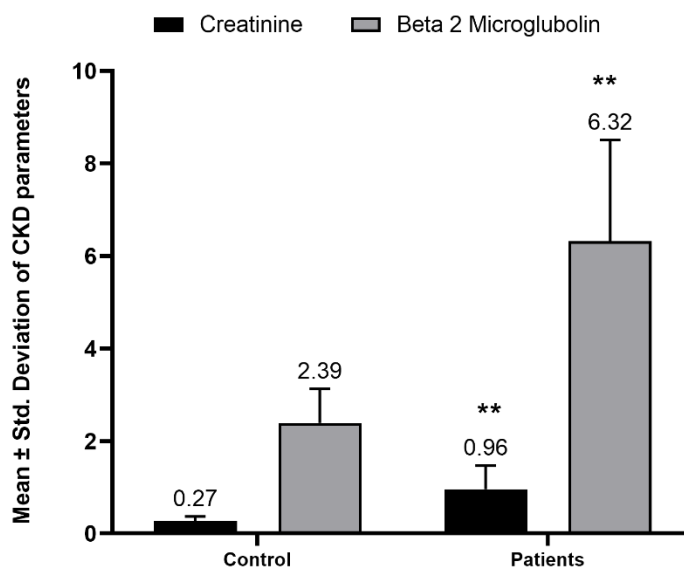


Fig. 2. The Comparison of serum Creatinine and Beta 2 Macroglobulin Level within patients suffering CKD and their corresponding controls.

**4.3 Relationship of IL-17A with CKD parameters**

The association investigation that was performed between the level of serum creatinine and IL-17A as well as Beta 2 Macroglobulin and IL-17A for those who were diagnosed with CKD is illustrated conveniently in Figure 3 and Figure 3, respectively. Additionally, the results obtained exhibit a statistically significant association between the serum creatinine and IL-17A, with a p-value of 0.001 and a correlation coefficient (r) of 0.411, which is below the conventional significance threshold of 0.05. Moreover, there has been a statistically significant association between the serum Beta 2 Macroglobulin and IL-17A, with a p-value of 0.001 and r value of 0.411. Therefore, the present study evaluates both the magnitude and the direction of the association between the CKD biochemical indicators (creatinine, Beta 2 Macroglobulin) and IL-17A, which emphasizes their potential connections within the context of CKD.

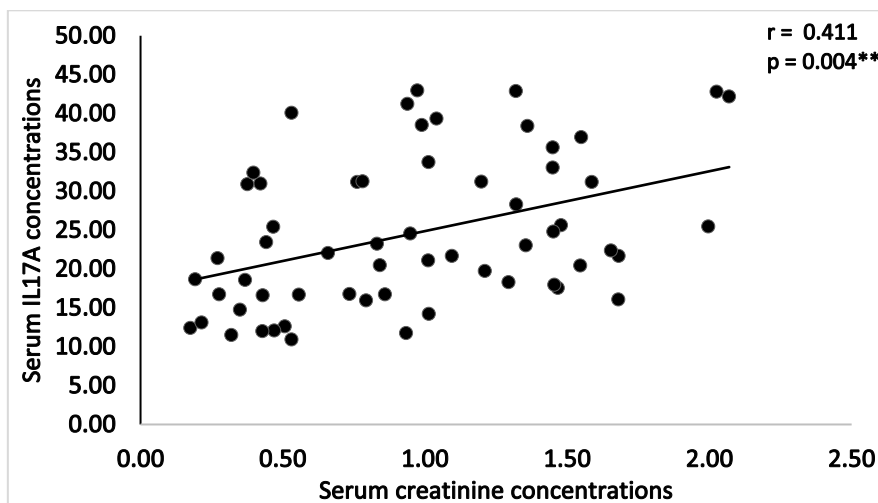


Fig. 3. The Correlation Coefficient between serum Creatinine and IL-17A concentrations in patients with CKD.

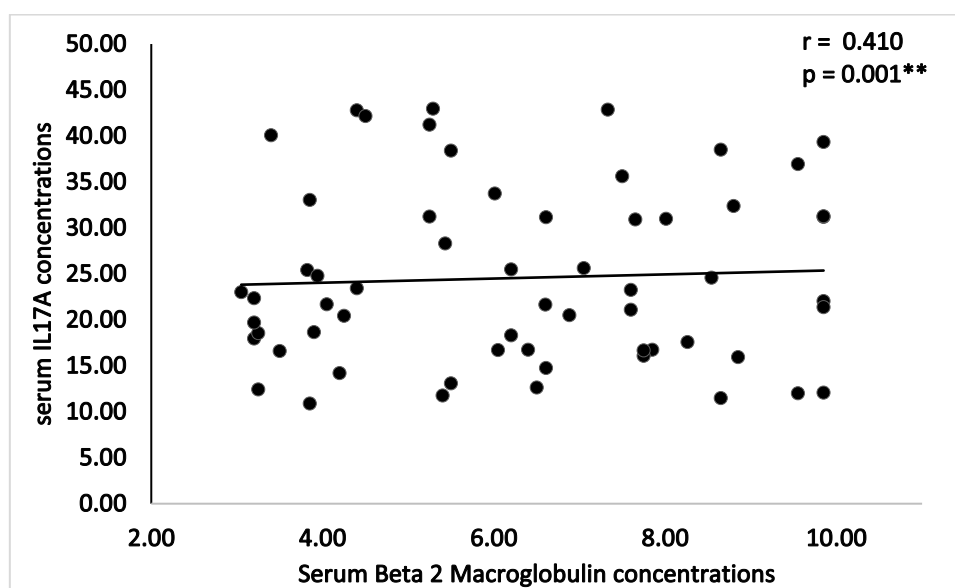


Fig. 4. The Correlation Coefficient between serum Beta 2 Macroglobulin and IL-17A concentrations in patients with CKD.

**5. Discussion**

Failure of the renal system is a condition that arises when the kidneys have no ability to filter out waste from the body's metabolic processes or to fulfill its regulatory function [30]. It is possible for advanced chronic renal disease to produce a decrease in urine excretion, which might result in an accumulation of metabolites such as electrolytes, urea, creatinine, and water in the human body [31]. More importantly, IL-17A is a critical cytokine that plays a role in the regulation of immune response and inflammation. Inflammation that is persistent is a characteristic of CKD, and its increased levels in people with CKD may result in chronic inflammation and increase renal damage. Chronic inflammation that has been caused by IL-17A might have an effect on the state of health of the vascular system,

increase fibrosis more serious, and make complex conditions which are frequently associated with CKD worse, including cardiovascular disease.

In the current investigation, the fact that IL-17A levels have been shown to be higher among those who had CKD implies that it may have the ability to exist as a biomarker for the development or severity of the medical condition. The pro-inflammatory cytokine referred to as IL-17A may be a factor in the systemic inflammation that typically occurs in CKD. likewise, the high levels of this substance might be considered as a potential target for therapeutic treatments in order to minimize inflammation and the challenges that are linked to it in these individuals. An intriguing observation is that the variability in IL-17A levels is significantly higher for those with CKD ( $24.56 \pm 9.60$  pg/mL) as compared with the control group ( $5.65 \pm 1.84$  pg/mL). These variations might be a result of variances in the stage of the disease, comorbidities, or particular patient conditions. Because of this variety, it is crucial to take a tailored approach to comprehending and controlling the important role that IL-17A plays in CKD. These outcomes are compatible with those of several studies of other research [29], [30], [32], [33]. In addition, high levels of IL-17A have a possibility to fulfill the role of a biomarker for inflammation and the severity of the medical conditions, while also offering chances for medical treatment.

Nevertheless, creatinine as well as beta 2 macroglobulin are adequate biomarkers for kidney conditions, and it is frequently utilized in the measurement of the eGFR, which offers a more thorough evaluation of renal health. Creatinine and Beta 2 Macroglobulin are a vital indicator to assess the effectiveness of renal filtration, and higher creatinine levels in individuals with chronic kidney disease are indications of decreased kidney function. The higher level of differences seen in the patient group ( $0.96 \pm 0.51$  mg/dL) in comparison to the control group ( $0.27 \pm 0.10$  mg/dL) of the creatinine and ( $2.39 \pm 0.74$  mg/dL) in comparison to the control group ( $6.32 \pm 2.19$  mg/dL) of the beta 2 macroglobulin implies that there may be heterogeneity in the level of renal failure or additional factors that influence it, such as comorbidities and treatment regimens.

Therefore, the present work highlights the crucial role of creatinine as a key biomarker for the diagnosis and monitoring of CKD. The noticeable increase in creatinine levels within CKD patients points out kidney function issue and reinforces its ongoing application as a diagnostic measure in medical arena. Therapeutic factors include monitoring creatinine levels regularly to assess the effectiveness of treatments designed to preserve kidney function or slow the development of CKD. In a similar manner increased levels could guide interventions including dietary changes, hydration approaches, and medication adaptations.

The observation of a moderate positive association between IL-17A levels and CKD biomarkers, such as creatinine and Beta 2 Macroglobulin, indicates that IL-17A could be significantly related to the chronic inflammation associated with CKD. There are several kinds of immune cells, particularly T-helper 17 (Th17) cells, that are responsible for the production of IL-17A. This cytokine is known to have a role in immune responses that are innate as well as adaptive. In light of chronic kidney disease, increased levels of IL-17A might boost inflammatory pathways that contribute to kidney damage, fibrosis, and complications including cardiovascular disease. Given the established evidence indicating that IL-17A acts as a pro-inflammatory cytokine, there's a chance it serves as a contributor in the broader inflammation seen in CKD. This might result in vascular impairment leading to a decline in renal activity which can cause hypertension and atherosclerosis. Furthermore, the relationship which was

established may provide evidence supporting the idea that IL-17A is a good candidate for the progression of CKD.

An increase in IL-17A levels, which reflects a deterioration of renal function as evidenced by elevated creatine levels, may signify the progression of the pathology. These levels could be used to evaluate the inflammatory state of CKD patients thereby reflecting the degree of inflammation of the kidneys and possibly providing guidance as to how best to treat the inflammation. This progression of the disease may in fact be monitored by tracking levels of IL-17A. Furthermore, since IL-17A is implicated in various autoimmune and inflammatory diseases, its increased levels in CKD patients may reflect a broader immune dysregulation, contributing to the worsening prognosis of these patients.

### Conclusion

This study demonstrates a significant correlation between increased blood IL-17A levels and impaired renal function in individuals with CKD. The higher levels of IL-17A noticed in CKD patients point to its probable involvement in the inflammatory mechanisms that worsen kidney damage and lead to the systemic issues usually associated with CKD. In a similar vein, the remarkable rise in serum creatinine and beta 2 macroglobulin levels among these persons indicates the kidney impairment which is characteristic of CKD. Also, the marked correlation between the concentrations of IL-17A and CKD markers in patients verifies the fact that IL-17A is a cytokine that is driven by inflammatory agents that cause the deterioration of kidney function. Also, creatinine and beta-2 microglobulin are key parameters to evaluate kidney function and to analyze the evolution of the pathology. More studies are required to investigate the effectiveness of inhibiting IL-17A for the management of chronic kidney disease and determine its role in pathology development.

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