

## ORIGINAL ARTICLE

# A Key Role of Interleukin 34 in Patients with Chronic Kidney Disease and Lupus Nephritis

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## ABSTRACT

### Key words:

Interleukin34, Kidney disease, Lupus nephritis

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**Background:** Chronic kidney disease is a progressive condition characterized by the gradual loss of kidney function over time. It is a significant public health issue, with a prevalence estimated to be between 9-15 % worldwide. **Objective:** This study investigates the relation between IL-34 and chronic kidney disease with lupus nephritis. **Methodology:** The study included 35 healthy controls, 35 patients with chronic kidney disease, and 35 patients with chronic kidney disease and lupus nephritis who were hospitalized in ALNajaf Hospital between September 1, 2023, and January 1, 2024. ELISA has been used to assess interleukin-34 and antinuclear antibody in each person's serum. **Results:** The results proved that there was a significant increase ( $P$  value $<0.0001$ ) in serum levels of anti-nuclear antibodies in patients ( $9.158 \pm 0.448$  pg/ml) compared with control ( $0.2475 \pm 0.017$  pg/ml). Also, there was a higher serum levels ( $P$  value $<0.0001$ ) in patients with chronic kidney disease and lupus nephritis patients as compared with chronic kidney disease patients. Patients' levels of interleukin-34 were substantially higher ( $P<0.05$ ) than those of control participants. People with lupus nephritis had significantly different blood levels of antinuclear antibodies ( $P<0.05$ ). **Conclusion:** IL-34 has an important role in patients with chronic kidney disease with lupus nephritis.

## INTRODUCTION

Chronic kidney disease (CKD) is a prevalent health condition that poses a significant threat to human well-being<sup>1</sup>. It can lead to complications such as end-stage renal disease, requiring hemodialysis as the main treatment option for affected individuals. Additionally, the high healthcare costs associated with chronic kidney disease highlight the urgent need for awareness, prevention, and effective management strategies. Furthermore, the impact of chronic kidney disease extends beyond its direct effects on kidney function<sup>2,3</sup>.

It is also a major risk multiplier for other chronic diseases, including diabetes, hypertension, heart disease, and stroke<sup>4</sup>. As such, addressing chronic kidney disease is crucial not only for improving individual health outcomes but also for reducing the burden on healthcare systems and promoting overall public health<sup>5</sup>. It is essential to use the above sources responsibly and to avoid directly plagiarizing them when discussing chronic kidney disease and its impact on public health<sup>6,7</sup>.

It occurs when the immune system attacks the kidneys, leading to inflammation and damage<sup>8</sup>. The severity of lupus nephritis can vary with different forms identified based on clinical features and progression. Some common symptoms of lupus nephritis include proteinuria, high blood pressure, and decreased kidney

function<sup>9</sup>. Treatment of lupus nephritis typically involves a combination of medications, such as corticosteroids, immunosuppressants, and angiotensin receptor blockers, to reduce inflammation and protect the kidneys from further damage. Regular monitoring of kidney function and managing any underlying lupus activity are also important components of managing lupus nephritis<sup>10,11</sup>.

IL-34 is a cytokine that has been implicated in the pathogenesis of lupus nephritis, a severe kidney inflammation associated with systemic lupus erythematosus. Understanding the mechanisms by which IL-34 affects lupus nephritis can lead to the development of novel therapies aimed at mitigating renal damage and improving patient<sup>12,13</sup>.

## METHODOLOGY

### Patients

A total of 120 individual with the age range (18-60) years are enrolled in this study that was carried out in Department of Nephrology at AL-Najaf Hospital in AL-Najaf City, Iraq from 1<sup>st</sup> August 2023 to the end of December 2024. 35 individuals infected with CKD, 35 individuals infected with chronic-kidney disease-lupus nephritis and 35 healthy individuals have a negative history and no clinical evidence of any other disease as

control. All CKD and LN- patients have been clinically diagnosed by the physicians.

**Measurement of serum levels of IL-34 and antinuclear antibody**

Five milliliters of blood were taken from each subject, and two milliliters of serum were recovered by centrifugation at 8000 rpm/10 minutes<sup>14,15</sup>. The enzyme-linked-immunosorbent-assay was used to quantify IL34 and antinuclear antibody based on serum concentration as follow<sup>16,17</sup>: after the determination of diluted standard, blank, and sample wells, 100 µL each dilution were added, and the micro-ELISA plate was covered by the sealer and incubated for 90 min at 37°C. After incubation, all liquid was removed from each well, 100 µL of Bio-tinylated detection antibody solution were added to each well, and the micro-plate was covered with a new sealer and incubated for 1 hour at 37°C . After incubation, all liquid was removed from each well and washed by adding 350 µL of washing buffer to each well (these steps were repeated three times). 100 µL of HRP Conjugate working solution were added to each well, covered by a micro-plate and incubated at 37°C for 30min.The solution was removed from each well, and the washing step was repeated five times. Then 90 µL of substrate reagent were added to each well, and the micro-plate was covered by micro-plate sealer and incubated for 15 min. at 37°C. 50 µL of stop solution were added to each well, and determination of the optical density (OD value) was done by ELISA reader at 450nm wavelength, then the results were calculated by plotting the standard curve.

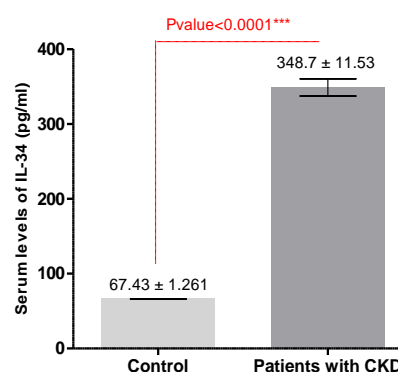
**Statistical analysis**

It was performed using (graph-pad-prism), and a mean value and standard error (SE) were calculated for each value. The statistical analysis took into account statistically-significant *P* values of less than 0.05<sup>18,19</sup>.

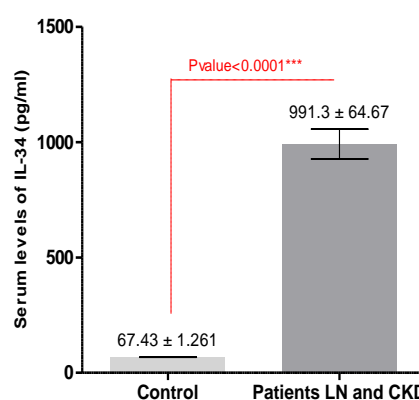
**RESULTS**

**IL-34**

A significant increase (*P* value<0.0001) in serum levels of IL-34 in CKD-patients was higher (348.7±11.53 pg/ml) compared with control (67.43±1.261 pg/ml) (Figure 1). Also, the results showed a higher serum levels in CKD-LN-patients (991.3±64.67 pg/ml) compared with the control with a significant increase was recorded (*P* value <0.0001) (Figure 2). A significant increase (*P* value <0.0001) was recorded also in IL-34 serum levels of CKD-patients was seen compared with CKD-LN-patients (Table 1).



**Fig. 1:** Serum levels of IL-34 in healthy individuals and CKD-patients



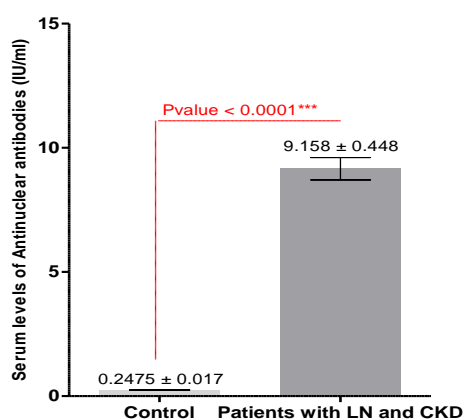
**Fig. 2:** Serum levels of IL-34 in healthy individuals and CKD-LN-patients

**Table 1:** CD163 blood levels in CKD-patients and CKD-LN-patients

Serum levels of IL-34 (pg/ml)		P-value
Patients with CKD	Patients with LN and CKD	< 0.0001 Significant
348.7 ± 11.53	991.3 ± 64.67	

**Antinuclear antibody**

There was a significant increase (*P* value<0.0001) recorded in serum levels of anti-nuclear antibodies in CKD-LN-patients (9.158±0.448 pg/ml) compared with the control (0.2475±0.017 pg/ml) (Figure 3). Also, there was a higher serum levels (*P* value <0.0001) in CKD-LN-patients when compared with CKD-Patients (Table 2).



**Fig.3:** Anti-nuclear antibodies concentration in healthy individuals and CKD-patients

**Table 2: Serum levels of anti-nuclear antibodies in individuals infected with chronic kidney disease and lupus nephritis**

Serum levels of anti-nuclear antibodies (IU/ml)		P-value
Patients with CKD	Patients with CKD and LN	< 0.0001*** Significant
0.2575±0.01597	9.158 ± 0.4489	

## DISCUSSION

Interleukin34 plays an important role in the immune responses and inflammation. Anti-nuclear antibodies are autoantibodies that target nuclear antigens in cells<sup>20</sup>.

By examining the relationship between IL-34 and anti-nuclear antibodies, potentially develop novel therapeutic approaches targeting IL-34 to modulate immune responses and alleviate autoimmune symptoms<sup>21</sup>.

Additionally, the detection and measurement of IL-34 and anti-nuclear antibodies may serve as a diagnostic tool to identify individuals at risk for developing autoimmune diseases or monitor the progression of existing conditions.

IL-34 is an important cytokine is produced in cases with lupus nephritis, which is a severe form of kidney inflammation caused in individuals with systemic lupus erythematosus<sup>22</sup>.

Researchers have found that IL34 in the kidneys of lupus nephritis patients contributes to the recruitment and activation of immune cells<sup>23</sup>.

Lupus nephritis could potentially manage this debilitating condition. Further studies are needed to fully elucidate the precise mechanisms by which IL-34 influences the pathogenesis of lupus nephritis and how it can be targeted for treatment<sup>24</sup>.

Additionally, targeting IL-34 may provide potential opportunities for personalized medicine in the management of lupus nephritis as it could allow for tailored interventions based on an individual's IL-34 levels and immune response<sup>25</sup>.

The research on IL-34 and its association with lupus nephritis could pave the way for better understanding and treatment of this complex kidney condition. Furthermore, investigating the role of IL-34 in lupus nephritis may also help unravel the underlying factors contributing to disease heterogeneity and different clinical manifestations in patients with lupus nephritis<sup>26</sup>.

Understanding the interplay between IL-34 and anti-nuclear antibodies holds great potential for improving our understanding, diagnosis, and treatment of autoimmune diseases<sup>27</sup>.

IL-34 anti-nuclear antibodies have the potential to revolutionize our understanding and treatment of autoimmune diseases<sup>28</sup>. They have the potential to provide valuable insights into the development and progression of autoimmune disorders<sup>29,30</sup>.

## CONCLUSION

In patients, IL-34 and anti-nuclear antibodies levels were significantly elevated. The immune markers IL-34 can be used for early diagnosis of kidney infections.

## Ethical Consideration

It was approved by the Institutional Ethics-Committees at the University of Kufa and the Scientific-Committee for Research in the Health Department of Najaf. Iraq.

## Declarations:

**Consent for publication:** Not applicable

**Availability of data and material:** Data are available upon request.

**Competing interests:** The author(s) declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article. This manuscript has not been previously published and is not under consideration in another journal.

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