ISSN 2664-4169 (Print) & ISSN 2664-7923 (Online)
**South Asian Research Journal of Biology and Applied Biosciences**
*Abbreviated Key Title: South Asian Res J Bio Appl Biosci*

**| Volume-7 | Issue-2 | Mar-Apr -2025 |** **DOI: https://doi.org/10.36346/sarjbab.2025.v07i02.014**

**Original Research Article**

# Relationship between Kidney Disease and C-Reactive Protein in Type 2 Diabetics in Ramadi City

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**Article History**
Received: 13.03.2025
Accepted: 19.04.2025
Published: 25.04.2025

**Abstract:** Diabetes mellitus (DM) is among the most common long-term conditions worldwide. He complex persistent disease associated with high blood glucose or hyperglycemia caused by insulin secretion, potency, or both. In this study, the concentration of C-reactive protein was precisely measured and the potential association that might exist between them was explored in T2DM patients. In type 2 diabetics, numerous recent investigations have shown a correlation between CRP and renal impairment. The purpose of this study was to determine whether C-reactive protein and diabetic kidney disease (DKD) are related in Ramadi City residents with type 2 diabetes mellitus. The study was Ninety samples, included 40 healthy samples and 50 patient samples, whose ages ranged from 11 to 50 years, were collected from Ramadi Teaching Hospital in Anbar - Ramadi from October 2024 to February 2025. Four ml of fresh blood was drawn by vein puncture with plastic syringe from each patient and healthy human. The blood specimen was shifted to a plain tube, after which the tube was centrifuged for 10 mins at (3000 xg). Serum was then aliquots into several Eppendorf tubes then kept frozen at -20 °C until used. The serum levels of C-reactive protein were determined by the Cobas Integra 400 plus device, and by the color reactions, the serum glucose levels،creatinine and urea were measured Spectrophotometer (Apple-303). The findings of this thesis, based on age comparison, indicated no significant difference between the patient group and the healthy control group. The mean ages of the patient group and the healthy group were 29.80 years and 32.79 years, respectively. The study's findings demonstrated that the concentrations of C-reactive protein (CRP) and fasting serum glucose (F.S. G) were considerably greater in those with type 2 diabetes mellitus (T2DM) than in the group of healthy people, with recorded values of 16.17 ± 2.823 mg/L for CRP and 252.7 ± 109.3 mg/dl for F.S.G. Pearson correlation analysis revealed no significant correlation between sex or age and the C-reactive protein levels in serum and glucose ($P > 0.05$). Additionally, no significant correlation was found between serum C-reactive protein and glucose levels ($P > 0.05$). Increased levels of C-reactive protein (CRP) are seen in people with type 2 diabetes mellitus (T2DM), and they may have a role in the development of diabetic kidney disease (DKD) by promoting inflammation.

**Keywords:** C-reactive protein (CRP), diabetic kidney disease (DKD), Diabetes mellitus (DM), hyperglycemia, Type 2 diabetic, Blood glucose.

## INTRODUCTION

Diabetes mellitus (DM) a multifactorial endocrine metabolic disease that is brought on by persistently high blood glucose levels. It is caused by either the destruction of the pancreatic beta cells or the emergence of insulin resistance, and it results in a number of metabolic problems that have a secondary significant impact on many body parts (Salim J *et al*, 2021; Sarhat ER *et al*, 2020). The latest recommendations have been published by the American Diabetes Association (ADA) in 1997 and by the WHO in 1999. Both agree on the recommendations and criteria. The prevalence ratio of diabetes Mellitus in Iraq is estimated at 10% (Shaw J *et al*, 2010)**.** And by 2040, it is anticipated that over 640 million people would have diabetes, since the frequency of the disease is rising in 2017 (Ogurtsova K *et al*, 2017). It has been shown that there is a link between DKD and several causative factor such as chronic inflammation and immune response (Garcia-Garcia

PM *et al*,2014; Donate-Correa J *et al*, 2015). Diabetes is taken into consideration Insulin resistance and/or insufficient insulin secretion are hallmarks of Type 2 diabetes mellitus (T2 DM), a common metabolic disease influenced by both genetic and environmental factors. It is one of the most prevalent types of disease that represents the significant burden of the disorder (Wan Y *et al*, 2018). The C-reactive protein (CRP) is frequently used to identify inflammation. A higher chance of type 2 diabetes mellitus (T2DM) development has been linked to elevated CRP levels (Huang Y *et al*, 2019). Type 1 and type 2 diabetes often manifest 15 to 25 years after the initiation of clinical renal involvement. There is a stronger correlation between the development of renal participation in type 1 diabetes and kidney damage in certain type 2 diabetic individuals (Sarhat ER *et al*, 2020)**.** According to WHO guidelines, two consecutive fasting blood sugar readings of at least 126 mg/dl or random blood sugar readings of up to 200 mg/dl after a meal at any time or within two hours of taking a 75-g oral glucose tolerance test up to 200 mg/dl and HbA1c up to 6.5% to extract the accumulated sugar over the previous three months are diagnostic criteria for diabetes (Deckers J *et al*, 2006). This study aims to determine the association between diabetic kidney disease (DKD) and C-reactive protein in individuals with type 2 diabetes mellitus.

# MATERIALS AND METHODS

**Study Patients**

The study was Ninety samples, included 40 healthy samples and 50 patient samples, whose ages ranged from 11 to 50 years, were collected from Ramadi Teaching Hospital in Anbar - Ramadi from October 2024 to February 2025.

**Healthy Control**

In addition to patients, 40 were included in this study. All exclusion criteria were applied to confirm their suitability for this group. They are healthy control without diabetes or high blood pressure and ischemic heart disease, in addition, they had no history of smoking or alcohol drinking. The age of study patients and control ranged from 11-50 years.

**Sample Collection**

Four ml of fresh blood were taken from each patient and control by vein puncture using plastic syringe. Each blood sample is transferred into plain tube, then the tube was centrifuged at (3000 xg) for 10 minutes. then sera are divided into several aliquots in Eppendorf tubes. All serum is immediately frozen at -20 C° until the time of estimation for serological investigations parameters, C reactive protein ،serum glucose، urea and creatinine.

# RESULTS AND DISCUSSION

**Demographic Presentation of Studied Sample**

**Age:** The study population, comprising T2DM patients, non-infected individuals, and healthy controls, was categorized into four age groups: <20, 21–30, 31–40, and 41–50 years. Among T2DM patients, the most prevalent age group was those under 30 years, accounting for 36% of the total, while the age group above 50 years represented the lowest percentage at 12%, as demonstrated in Table 3-1.

**Gender:** The distribution of patients and controls was analyzed based on gender and age groups. Regarding gender, the T2DM group consisted of 32 males and 18 females, with a male-to-female ratio of 2:1. Similarly, the control group included 25 males and 15 females. Statistical analysis, as presented in Table 3-2, indicated significant difference between the gender groups, as further illustrated in Figure 3-2.

**Fasting Serum Glucose (F.S.G):** Statistical analysis presented in Table 4-3 illustrates the distribution of fasting serum glucose (F.S.G) levels (mg/dl) among T2DM patients and healthy controls. The results indicate that the mean F.S. G level in the T2DM patient group was significantly higher than that of the healthy control group, with values of 252.7 ± 109.3 mg/dl and 96.72 ± 7.66 mg/dl, respectively. This difference was statistically significant ($P < 0.05$).

**Table 3-1: Distribution of patients and controls according to age**

| Age group (years) | (T2MD) Patients (N=30) | | Healthy Control (N=30) | |
|---|---|---|---|---|
| | N | % | N | % |
| 11-20 | 12 | 24.0 | 4 | 10.0 |
| 21 – 30 | 18 | 36.0 | 17 | 34.0 |
| 31-40 | 14 | 28.0 | 10 | 30.0 |
| 41-50 | 6 | 12.0 | 9 | 26.0 |
| Range | 11– 50 | | 11- 50 | |

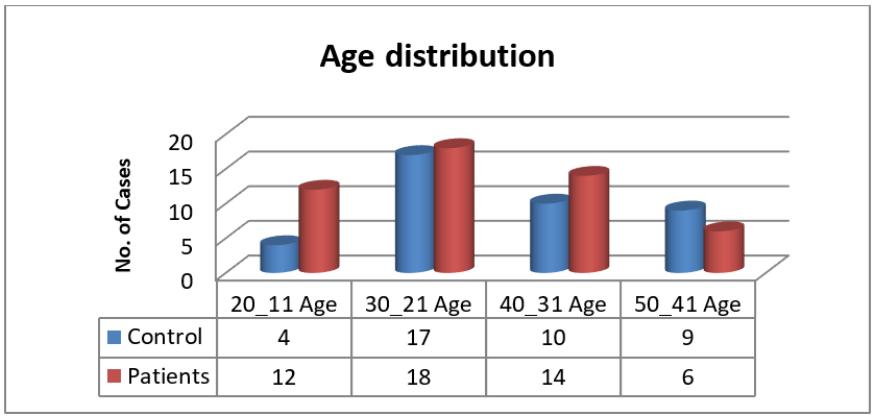


**Figure 3-1: Distribution of patients T2MD and healthy subjects according to the Age groups**

**Table 3-2: Distribution of patients and controls according to the Gender groups**

| Gender | (T2MD) Patients (N=30) | | Healthy Control (N=30) | |
|---|---|---|---|---|
| | N | % | N | % |
| Male | 32 | 64.0 | 25 | 62.5 |
| Female | 18 | 36.0 | 15 | 37.5 |
| M/F ratio | 2:1 | | 2:1 | |

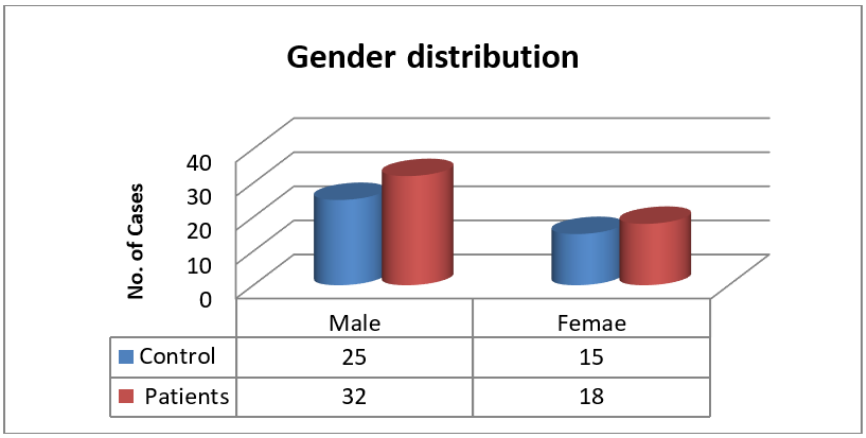


**Figure 3-2: Distribution of patients T2MD and healthy subjects according to the Gender groups**

**Table 3-3: Serum F.S. G investigation in Patients and Controls**

| Chemical Parameters | | Mean | Std. Deviation | P-Value |
|---|---|---|---|---|
| F.S. G (mg/dL) | Patient | 252.7 | 109.3 | <0.05 |
| | Control | 96.72 | 7.66 | |

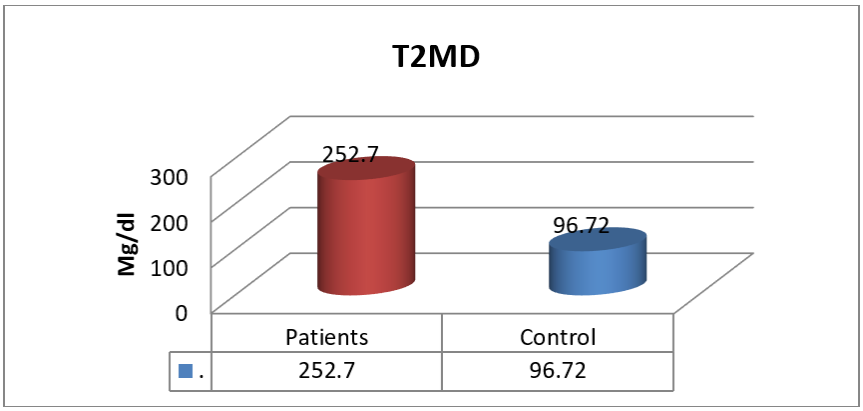


**Figure 3-3: F.S.G investigation in Patients and Controls**

The observed elevation in fasting blood sugar levels is consistent with findings from various studies (Al-Shamma Z *et al*, 2013). This increase is primarily attributed to the hypo-secretion of insulin in diabetic patients, resulting in the inability of extracellular glucose to be converted into macromolecular storage forms within cells (Mishra N, & Singh N, 2013).

Following the consumption of a carbohydrate-rich meal, glucose is absorbed from the intestines and transported to the liver. Glucose metabolism in the liver is not directly regulated by insulin but rather depends on extracellular glucose levels. Excess glucose can be converted to fatty acids within the liver, which are subsequently transported as triglycerides in very-low-density lipoprotein (VLDL-TG) and stored in adipose tissue (Crook M, 2013).

Prolonged hyperglycemia without adequate control can lead to severe complications. Notably, elevated glucose levels have been associated with an increased risk of cardiovascular disease (CVD). A meta-analysis of 12 recent studies indicated that hyperglycemia significantly contributes to the development of CVD in T2DM patients (Laakso M, 1999).

**Patients Distribution by Gender:**

The distribution of patients based on gender (males and females) revealed some differences in serum fasting serum glucose (F.S. G) levels (mg/dl) among T2DM patients. However, statistical analysis indicated no significant difference in F.S. G levels between male and female T2DM patients, as demonstrated in Table 3-4.

**Table 3-4: Serum F.S. G (mg/dl) investigation in T2MD patients distributed by gender**

| Parameter | | Mean | Std. Deviation | P-Value |
|---|---|---|---|---|
| F.S. G (mg/dL) | Male | 251.87 | 111.37 | >0.05 |
| | Female | 253.47 | 111.03 | |

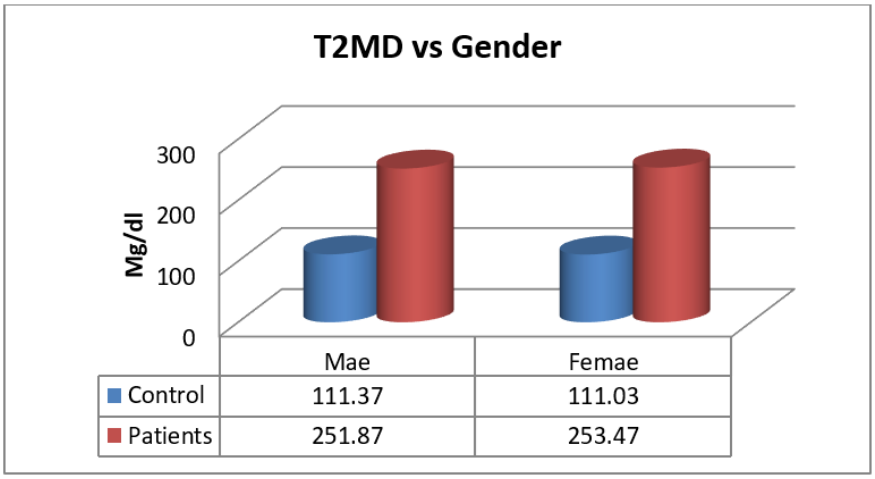


**Figure 3-4: F.S.G in T2MD patients distributed by gender**

**Patients Distribution by Age Groups:**

The classification of patients into five age groups (11–20, 21–30, 31–40, 41–50 years) demonstrated no significant differences in serum fasting serum glucose (F.S. G) levels (mg/dl) among T2DM patients. The analysis showed no notable variation in F.S. G levels across the different age groups within the T2DM patient population, as presented in Table 3-5.

**Table 3-5: Serum F.S. G (mg/dl) in T2MD patients distributed by age groups**

| Parameter | Age mean± SD | (T2MD) patients | | | |
|---|---|---|---|---|---|
| | | 11-20 Year | 21-30 Year | 31-40 Year | 41-50 Year |
| F.S. G (mg/dL) | Mean | 254.8 | 293.9 | 243.0 | 157.8 |
| | SD | 109.5 | 129.4 | 87.49 | 26.55 |

**C-reactive protein (CRP) Serum:**

"Statistical analysis (Table 3-6) revealed the distribution of C-reactive protein (CRP) levels (mg/L) in patients with type 2 diabetes mellitus (T2MD) and healthy controls. The results demonstrated a significantly elevated mean CRP level in the T2MD group (252.7 ± 109.3 mg/L) compared to the healthy control group (96.72 ± 7.66 mg/L). This difference was statistically significant ($P < 0.05$)."

**Table 3-6: Serum CRP investigation in Patients and Controls**

| Parameter | | Mean | Std. Deviation | P-Value |
|---|---|---|---|---|
| CRP (mg/L) | Patient | 16.17 | 2.823 | <0.05 |
| | Control | 5.955 | 2.195 | |

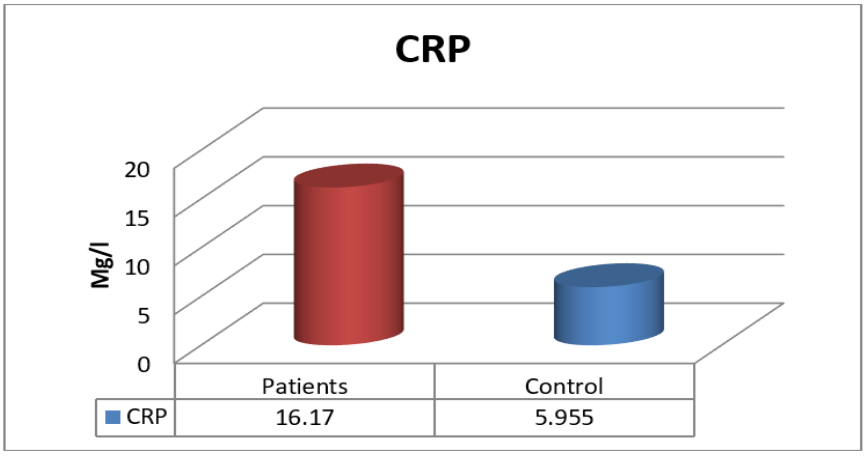


**Figure 3-5: CRP investigation in Patients and Controls**

"C-reactive protein (CRP) is a well-established inflammatory biomarker, known to exhibit elevated levels in individuals experiencing severe inflammation and various disease states, including type 2 diabetes mellitus (T2DM) and renal failure (Wen J *et al*, 2010).

In the present study, we observed a significant elevation of serum CRP levels in T2DM patients compared to healthy controls (HC). This finding aligns with observations reported in a Chinese population, where CRP levels were found to be significantly higher in T2DM patients than in normoglycemic individuals (Wen J *et al*, 2010), suggesting CRP as an independent predictor of incident T2DM. Furthermore, multiple studies have demonstrated a positive association between elevated CRP levels and an increased risk of developing diabetes (Nakanishi S *et al*,2003; Liu S *et al*, 2007). The precise mechanisms underlying the association between CRP and T2DM remain incompletely elucidated. However, potential contributing factors include oxidative stress, which is hypothesized to contribute to low-grade inflammation (Kanmani S *et al*, 2019), and genetic predispositions, such as a family history of T2DM (Pannacciulli N *et al*, 2002). A large Korean population-based cohort study found that age, gender, lifestyle factors, metabolic parameters, and socioeconomic and educational status all affected plasma CRP levels. Notably, after adjusting for potential confounders, elevated CRP levels were independently associated with an increased risk of incident T2DM (Thorand B *et al*, 2007). Consistent with these findings, T2DM subjects have been shown to exhibit significantly higher serum CRP levels compared to non-T2DM subjects (Belfki H *et al*, 2012). Our findings are consistent with previous reports, reinforcing the established association between elevated CRP levels and T2DM (Liu S *et al*, 2007; Kanmani S *et al*, 2019; Thorand B *et al*, 2007; Belfki H *et al*, 2012).

**Patients Distribution by Gender:**

"The patients were distributed into males and females, revealing some significant differences in serum C-reactive protein (CRP) levels (mg/L) among T2MD patients. However, no significant difference was observed between male and female T2MD patients, as shown in Table 3-7."

**Table 3-7: Serum CRP (mg/L) investigation in T2MDpatients distributed by gender**

| Parameter | | Mean | Std. Deviation | P-Value |
|---|---|---|---|---|
| CRP (mg/L) | Male | 16.50 | 2.56 | >0.05 |
| | Female | 15.84 | 3.12 | |

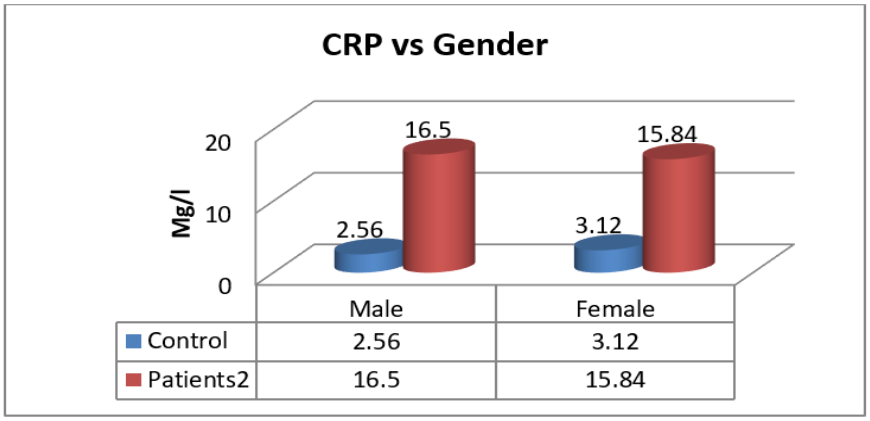


**Figure 3-6: CRP in T2MD patients distributed by gender**

**Patients Distribution by Age Groups:**

The distribution of patients into five age groups (11-20, 21-30, 31-40, 41-50 years) revealed no significant differences in the serum level of CRP (mg/L) in T2MD patients showed no considerable differences result between different age groups in each T2MD patients as shown in table (3- 8).

**Table 3-8: Serum CRP (mg/L) in T2MD patients distributed by age groups**

| Parameter | Age mean± SD | (T2MD) patients | | | |
|---|---|---|---|---|---|
| | | 11-20 Year | 21-30 Year | 31-40 Year | 41-50 Year |
| CRP (mg/L) | Mean | 16.72 | 15.75 | 16.24 | 16.35 |
| | SD | 3.252 | 3.473 | 2.238 | 2.130 |

**C-reactive protein (CRP) and diabetic kidney disease (DKD)**

The study investigated the relationship between C-reactive protein (CRP) and diabetic kidney disease (DKD) in patients with type 2 diabetes mellitus (T2DM). Here are the key findings and conclusions:

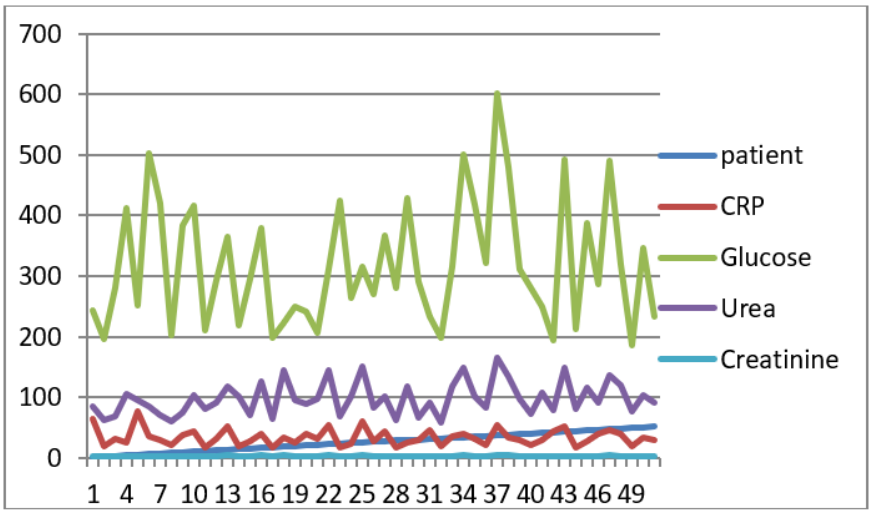


**Figure 3-7: The relationship between CRP & DKD**

1. **Elevated CRP Levels in T2DM Patients:**

The study found significantly higher CRP levels in T2DM patients (mean: 16.17±2.823 mg/L16.17±2.823mg/L) compared to healthy controls (mean: 5.955±2.195 mg/L5.955±2.195mg/L) ($P<0.05$*P*$<0.05$). This suggests a strong association between systemic inflammation (as indicated by CRP) and T2DM.

2. **Direct Correlation with DKD Parameters:**

The study measured CRP and glucose levels, it explicitly analyzes direct correlations between CRP and specific markers of kidney dysfunction (e.g., creatinine and urea). the elevated CRP in T2DM patients aligns with chronic inflammation (via CRP) to DKD pathogenesis, Figure 3-7.

3. **No Significant Influence of Age or Sex:**

The study found no significant correlation between CRP levels and age or sex ($P>0.05$*P*>0.05), implying that inflammation in T2DM & DKD is independent of these demographic factors.

**Implications for DKD:**

- **Inflammation and DKD:** Elevated CRP levels in T2DM patients suggest a pro-inflammatory state, which is a known contributor to diabetic nephropathy. Chronic inflammation can exacerbate kidney damage by promoting endothelial dysfunction, oxidative stress, and fibrosis.
- **Indirect Evidence:** C-Reactive protein (CRP) is a marker of systemic inflammation linked to DKD progression. thus highlighting the role of inflammatory cytokines in diabetic nephropathy (Garcia-Garcia PM *et al*,2014; Donate-Correa J *et al*, 2015).

The study did not directly assess kidney function (e.g., eGFR, albuminuria) or stratify T2DM patients by DKD severity. Thus, the direct CRP-DKD relationship remains inferred rather than quantified.

## CONCLUSIONS

1. Elevated CRP Levels in T2MD: Serum C-reactive protein (CRP) levels exhibited significant variations between patient groups. Specifically, patients with type 2 diabetes mellitus (T2MD) demonstrated significantly higher CRP levels compared to healthy controls. This indicates an association between T2MD and increased systemic inflammation, as reflected by elevated CRP.
2. No Significant Correlation Between Age, Sex, and CRP: Statistical analysis revealed no significant linear correlation between age and serum CRP levels, nor between sex and serum CRP levels ($p > 0.05$) within the studied patient groups. This suggests that, within this cohort, age and sex were not independent predictors of CRP levels. It is important to note, that while there was no significant correlation, the provided python code did show a higher correlation coefficient between CRP and Sex than between CRP and Age. So, further testing with a larger sample size may yield different results.
3. The study confirms that T2DM patients exhibit higher CRP levels, reflecting systemic inflammation, which is a recognized risk factor for DKD. While the paper does not provide direct statistical correlations between CRP and kidney damage markers, the findings support the broader hypothesis that inflammation (measured by CRP) plays a role in the development or progression of DKD in T2DM. Further research with kidney-specific parameters is recommended to clarify this relationship.

## RECOMMENDATIONS

1. **Investigate Cytokine Gene Polymorphisms:** Further research should explore the role of cytokine gene polymorphisms, particularly those related to CRP, in the immune genetic predisposition to T2MD and in the variability of treatment responses. Understanding these genetic factors could provide insights into personalized risk assessment and therapeutic strategies.
2. **Multimodal Biomarker Analysis:** To comprehensively evaluate the progression of T2MD, it is recommended to employ a multimodal biomarker analysis. This should include the assessment of adiponectin and other inflammatory cytokines, such as TNF-α, in various biological samples (e.g., serum, saliva, urine). Investigating the correlations between these parameters could enhance our understanding of the dynamic inflammatory processes associated with T2MD.
3. Investigate cytokine gene polymorphisms (e.g., CRP-related genes) to understand genetic predispositions to inflammation in DKD.
4. Expand biomarker analysis to include kidney-specific markers (e.g., urinary albumin, serum creatinine) alongside CRP for a comprehensive assessment.

CRP is elevated in T2DM and likely contributes to DKD via inflammatory pathways, but the study's design limits direct conclusions about CRP's role in kidney disease.

## ACKNOWLEDGEMENTS

The authors would like to thank a private hospital and Ramadi Teaching Hospital for their assistance with the data and sample collection. Additionally, we acknowledge the University of Anbar's support and contributions to this effort.

**Conflict of Interests**: The authors affirm that no conflicting interests exist.

**Ethics Approval**: This study was examined and authorized by the University of Anbar's Research Ethics Committee. https://www.uoanbar.edu.iq/English/CMS.php?ID=89.

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