

# Exploring Genetic Variations in KCNA10 and SLC13A3 Genes and Their Association in Chronic Kidney Disease in Southern Chennai Population

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## ABSTRACT

**Background:** Chronic kidney disease (CKD) is a progressive renal disorder influenced by both metabolic disturbances as well as genetic factors. Variations in the KCNA10 and SLC13A3 genes may contribute to an individual's risk of developing CKD, studies exploring these associations in the southern Chennai population. **Aim:** To evaluate the association of KCNA10 (rs34970857) and SLC13A3 (rs6066043) gene polymorphisms with CKD and their correlation with renal and biochemical parameters. **Methods:** A hospital-based cross-sectional study was conducted among 150 participants (75 CKD cases and 75 controls). Genotyping was performed using TETRA ARMS-PCR. Biochemical parameters including serum creatinine, BUN, eGFR, uPCR, HbA1c, lipid profile, calcium, phosphate and uric acid were analyzed. Statistical analysis was carried out using the chi-square test, and Multivariate logistic regression analysis. **Results:** The average age of the participants was comparable between the CKD cases ( $58.6 \pm 9.4$  years) and controls ( $57.8 \pm 9.6$  years;  $p=0.71$ ). Males were predominant in cases (66.7%,  $p=0.04$ ). Serum creatinine ( $6.65 \pm 2.01$  vs  $0.93 \pm 0.12$  mg/dL), BUN ( $71.8 \pm 8.9$  vs  $14.5 \pm 3.1$  mg/dL), and uPCR ( $4.2 \pm 1.4$  vs  $0.12 \pm 0.07$  mg/mg) were significantly higher in cases ( $p<0.001$ ), while eGFR was reduced ( $21.3 \pm 4.6$  vs  $97.8 \pm 6.5$  mL/min/1.73 m<sup>2</sup>). KCNA10 AA genotype showed increased risk (OR=2.19,  $p=0.02$ ). SLC13A3 AA genotype demonstrated strongest association (OR=5.39,  $p<0.001$ ). A significantly increased frequency of the A allele was observed among the cases for both genes. ( $p\leq 0.001$ ). **Conclusion:** Polymorphisms in KCNA10 and SLC13A3 genes are significantly associated with CKD risk. The A allele in both genes may serve as a potential genetic marker for susceptibility.

**Keywords:** Chronic Kidney Disease (CKD), Genetic Susceptibility, KCNA10 Gene Polymorphism, Renal Function Biomarkers, SLC13A3 Gene Polymorphism

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## INTRODUCTION

Chronic kidney disease (CKD) is a major global public health concern characterized by progressive and irreversible deterioration of renal function over time. It is defined by the presence of structural or functional abnormalities of the kidney persisting for more than three months, with significant implications for overall health (Levey et al., 2007). The burden of CKD has increased substantially over the past few decades, largely driven by the rising prevalence of diabetes mellitus, hypertension,

and aging populations. Epidemiological studies estimate that nearly 10–15% of the adult population worldwide is affected by CKD, with similar trends observed in India, where approximately 13–17% of individuals are impacted. This growing burden contributes significantly to morbidity, mortality, and healthcare costs, particularly due to its progression to end-stage kidney disease (ESKD), which necessitates dialysis or kidney transplantation.

The classification and staging of CKD have been standardized by the Kidney Disease: Improving Global

Outcomes (KDIGO) guidelines, which categorize CKD into five stages based on estimated glomerular filtration rate (eGFR) (Levey et al., 2007). This standardized approach has enhanced early detection, monitoring, and management of CKD across diverse populations. Early stages are often asymptomatic, leading to delayed diagnosis and increased risk of complications such as cardiovascular disease, anemia, mineral bone disorders, and metabolic imbalances (Nanayakkara et al., 2012). Importantly, cardiovascular complications are the leading cause of mortality in CKD patients, often occurring before progression to ESKD.

In recent years, there has been increasing interest in understanding the genetic basis of CKD. While traditional risk factors such as diabetes and hypertension play a critical role, genetic susceptibility has emerged as a significant contributor to disease onset and progression (Athuraliya et al., 2011). Single nucleotide polymorphisms (SNPs), which are the most common form of genetic variation, have been extensively studied for their role in influencing kidney function and susceptibility to renal diseases. Identifying such genetic variants may help in early risk prediction, personalized treatment strategies, and improved disease outcomes.

Among the genes implicated in renal physiology, KCNA10 and SLC13A3 have gained attention due to their roles in ion transport and cellular metabolism. The KCNA10 gene encodes a voltage-gated potassium channel involved in regulating membrane potential and cellular excitability, which may influence renal tubular function and electrolyte balance (Jayatilake et al., 2013). Alterations in potassium channel activity can disrupt cellular homeostasis and contribute to renal dysfunction. On the other hand, the SLC13A3 gene encodes a sodium-dependent dicarboxylate transporter that facilitates the uptake of metabolites such as citrate and succinate in renal tubular cells (Bandara et al., 2012). These metabolites are essential for energy metabolism and maintaining acid-base balance in the kidney.

Genetic polymorphisms in these genes, particularly SNPs such as rs34970857 in KCNA10 and rs6066043 in SLC13A3, have been investigated in relation to CKD susceptibility in certain populations (Chandrajith et al., 2011). These polymorphisms may influence gene expression or protein function, thereby affecting renal physiology and contributing to disease development. However, most of the available studies have been conducted in limited geographic regions, and there is a paucity of data from diverse Indian populations.

Given the genetic heterogeneity diversity across India, it is essential to explore population-specific genetic associations with CKD. Previous studies have highlighted the role of genetic variants in CKD of unknown etiology, particularly in regions such as Central India and Sri

Lanka (Wimalawansa, 2014). However, there is a notable gap in research focusing on the southern Chennai population, where dietary, and lifestyle factors may interact with genetic predisposition. Therefore, investigating the association between KCNA10 and SLC13A3 gene polymorphisms and CKD in this specific population is of significant importance. Such studies may contribute to a better understanding of disease mechanisms, enable early identification of high-risk individuals, and support the development of targeted therapeutic interventions. Ultimately, integrating genetic insights with clinical parameters could improve disease prognosis and help reduce the growing burden of CKD (Ileperuma et al., 2009).

## METHODOLOGY

This hospital-based cross-sectional analytical study was conducted in the Department of Biochemistry in collaboration with the Central Research Laboratory, Chettinad Academy of Research and Education (CARE), Chennai, India. Ethical approval was obtained from the Institutional Human Ethics Committee and written informed consent was obtained from all participants prior to enrollment.

The prevalence of Chronic Kidney Disease (CKD) in India has been reported to be 13%, according to recent epidemiological studies. Based on the participants were divided into two groups: Group 1: 75 Chronic kidney diseases patients and Group 2: 75 healthy individuals without any known renal or systemic disease serving as controls.

**Inclusion criteria:** Patients diagnosed with CKD having eGFR <60 mL/min/1.73 m<sup>2</sup> for more than 3 months and evidence of kidney damage such as proteinuria (uPCR > 0.2 mg/mg) for more than 3 months.

**Exclusion criteria:** Individuals with acute kidney injury, kidney transplantation, ESRD on dialysis, autoimmune kidney diseases, and polycystic kidney disease were excluded.

## STUDY PROCEDURE:

The demographic details of the study participants included in the study were obtained using a questionnaire. 5ml of the blood was collected from the study participants using 0.5M EDTA tubes and subsequently centrifuged at 3000 rpm for 5 minutes. The biochemical parameters which were analysed included Creatinine, BUN, RBS, HbA1c, Total protein, Albumin, Globulin, TC, Triglycerides (TG), high density lipoprotein (HDL) very low-density lipoprotein (VLDL), Calcium, phosphate, Uric acid were measured using automated analyser in Biochemistry central clinical laboratory. Urine protein creatinine ratio (uPCR), eGFR was calculated using formulas.

Genomic DNA was extracted from peripheral blood leukocytes, and the purity of the DNA was assessed. The tetra-primer amplification refractory mutation system-polymerase chain reaction (ARMS-PCR) was used to

genotype single-nucleotide polymorphisms (SNPs) of the KCNA10 and SLC13A3 gene. The PCR products were subsequently resolved by electrophoresis on 1% Agarose Gel and visualized the bands using ethidium bromide.

## RESULT:

| Parameters                          | Case<br>Mean $\pm$ SD | Control<br>Mean $\pm$ SD | P-value |
|-------------------------------------|-----------------------|--------------------------|---------|
| <b>Age (group distribution)</b>     |                       |                          |         |
| 40–50                               | 12 (16.0%)            | 14 (18.7%)               | 0.82    |
| 51–60                               | 28 (37.3%)            | 25 (33.3%)               | 0.65    |
| 61–70                               | 22 (29.3%)            | 22 (29.3%)               | 1.00    |
| >70                                 | 13 (17.3%)            | 14 (18.7%)               | 0.84    |
| BMI(kg/m <sup>2</sup> )             | 31.01 $\pm$ 2.11      | 28.14 $\pm$ 2.02         | <0.001* |
| Waist circumference (cm)            | 98.03 $\pm$ 7.97      | 86.95 $\pm$ 5.67         | <0.001* |
| Systolic BP (mmHg)                  | 139.08 $\pm$ 6.99     | 107.21 $\pm$ 8.36        | <0.001* |
| Creatinine (mg/dL)                  | 6.65 $\pm$ 2.01       | 0.93 $\pm$ 0.12          | <0.001* |
| BUN (mg/dL)                         | 71.8 $\pm$ 8.9        | 14.5 $\pm$ 3.1           | <0.001* |
| eGFR ( mL/min/1.73 m <sup>2</sup> ) | 21.3 $\pm$ 4.6        | 97.8 $\pm$ 6.5           | <0.001* |
| uPCR (mg/mg)                        | 4.2 $\pm$ 1.4         | 0.12 $\pm$ 0.07          | <0.001* |
| Calcium(mg/dL)                      | 7.8 $\pm$ 0.6         | 9.2 $\pm$ 0.8            | <0.001* |
| Phosphate(mg/dL)                    | 6.0 $\pm$ 0.7         | 4.2 $\pm$ 0.9            | <0.001* |
| Uric Acid(mg/dL)                    | 8.1 $\pm$ 1.1         | 5.3 $\pm$ 1.2            | <0.001* |
| RBS (mg/dL)                         | 164.5 $\pm$ 62.3      | 113.2 $\pm$ 29.4         | <0.001* |
| HbA1c (%)                           | 7.2 $\pm$ 1.8         | 5.6 $\pm$ 0.9            | <0.001* |
| Total Protein (g/dL)                | 5.0 $\pm$ 0.9         | 7.1 $\pm$ 0.6            | <0.001* |
| Albumin (g/dL)                      | 2.3 $\pm$ 0.5         | 4.2 $\pm$ 0.4            | <0.001* |
| Globulin (g/dL)                     | 3.2 $\pm$ 0.8         | 2.8 $\pm$ 0.3            | 0.002*  |
| Total Cholesterol (mg/dL)           | 219.4 $\pm$ 55.2      | 182.4 $\pm$ 32.5         | <0.001* |
| Triglycerides (mg/dL)               | 181.7 $\pm$ 70.1      | 135.6 $\pm$ 36.8         | <0.001* |
| HDL (mg/dL)                         | 36.9 $\pm$ 13.2       | 50.8 $\pm$ 8.2           | <0.001* |
| LDL (mg/dL)                         | 136.8 $\pm$ 44.5      | 95.4 $\pm$ 20.3          | <0.001* |
| VLDL (mg/dL)                        | 36.3 $\pm$ 14.2       | 24.1 $\pm$ 6.3           | <0.001* |

Table 1: Comparative Analysis of Age Group Distribution and Biochemical Parameters Among CKD Patients (Cases) and Control Subjects

There was no significant difference in age distribution between CKD patients and controls ( $p > 0.05$ ). However, CKD patients had significantly higher BMI, waist circumference, systolic blood pressure, serum creatinine, BUN, uPCR, phosphate, uric acid, RBS, HbA1c, total cholesterol, triglycerides, LDL, VLDL, and globulin levels ( $p < 0.05$ ). In contrast, eGFR, calcium, total protein, albumin, and HDL levels were significantly lower in CKD patients than controls ( $p < 0.001$ ). These findings indicate marked renal impairment, metabolic dysregulation, and dyslipidemia among CKD patients.

#### GENOTYPE AND ALLELE DISTRIBUTION OF KCNA10

The KCNA10 genotype distribution differed significantly between CKD cases and controls ( $p = 0.002$ ). The CC genotype was more frequent in controls (77.3%) than in cases (52.0%), whereas the AA genotype was more common in cases (33.3%) than controls (22.7%). The CA genotype was observed only in cases (14.7%). Similarly, allele frequency analysis showed a significantly higher frequency of the A allele in cases (40.7%) compared to

controls (22.7%), while the C allele was more frequent in controls (77.3% vs. 59.3%;  $p = 0.001$ ). These findings suggest that the A allele is associated with an increased risk of CKD, whereas the C allele may have a protective effect.

#### GENOTYPING RESULTS FOR KCNA10 (rs34970857) BY TETRA ARMS-PCR

The polymorphism was performed using the Tetra Amplification Refractory Mutation System-Polymerase Chain Reaction (Tetra ARMS-PCR) with allele-specific inner and outer primers. PCR amplification was carried out in a 20  $\mu$ L reaction mixture containing 2 $\times$  multiplex master mix, allele-specific primers, genomic DNA, and nuclease-free water. The PCR conditions included initial denaturation at 95°C for 15 min, followed by 32 cycles of 95°C for 30 s, 64°C for 1 min, and 72°C for 1 min, with a final extension at 72°C for 5 min. Amplified products were resolved by agarose gel electrophoresis, producing fragment sizes of 180 bp (C allele), 157 bp (A allele), and 283 bp (outer control fragment) for genotype determination.

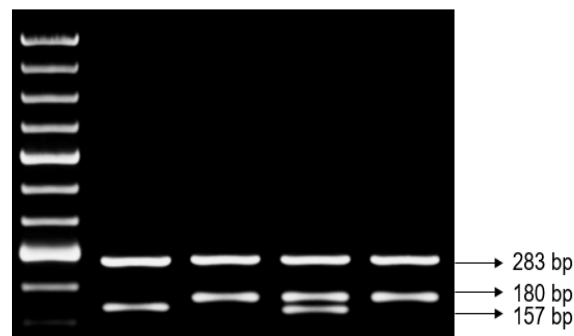


Figure : 1 Visualization of KCNA10 (rs34970857)

#### LOGISTIC REGRESSION ANALYSIS OF CKD VARIANTS – (KCNA10-RS34970857)

| Model             | Genotype / Allele | Cases n (%) | Controls n (%) | Odds Ratio (95% CI) | p-value |
|-------------------|-------------------|-------------|----------------|---------------------|---------|
| <b>Codominant</b> | CC                | 39(52.0%)   | 58 (77.3%)     | Reference           | 0.002*  |
|                   | CA                | 11(14.7%)   | 0 (0%)         | Not estimated       |         |
|                   | AA                | 25 (33.3%)  | 17 (22.7%)     | 2.19(1.05–4.59)     |         |
| <b>Dominant</b>   | CC                | 39(52.0%)   | 58 (77.3%)     | Reference           | 0.001*  |
|                   | CA + AA           | 36 (48.0%)  | 17(22.7%)      | 3.15 (1.57–6.32)    |         |
| <b>Recessive</b>  | CC + CA           | 50 (66.7%)  | 58 (77.3%)     | Reference           | 0.13    |
|                   | AA                | 25 (33.3%)  | 17 (22.7%)     | 1.71 (0.84–3.47)    |         |
| <b>Allelic</b>    | C                 | 89 (59.3%)  | 116 (77.3%)    | Reference           | 0.001*  |

|  |   |            |            |                  |  |
|--|---|------------|------------|------------------|--|
|  | A | 61 (40.7%) | 34 (22.7%) | 2.34 (1.42–3.84) |  |
|--|---|------------|------------|------------------|--|

Table 2: Logistic regression analysis of CKD variants – (KCNA10-rs34970857)

Logistic regression analysis demonstrated a significant association between the KCNA10 (rs34970857) polymorphism and CKD. Individuals carrying the CA + AA genotype had a 3.15-fold increased risk of CKD under the dominant model (OR = 3.15, 95% CI: 1.57–6.32;  $p = 0.001$ ). Similarly, the A allele was significantly associated with a 2.34-fold higher risk of CKD compared with the C allele (OR = 2.34, 95% CI: 1.42–3.84;  $p = 0.001$ ), indicating that the A allele is an independent genetic risk factor for CKD.

#### Association Analysis of KCNA10 (rs34970857)

The forest plot demonstrates that the KCNA10 (rs34970857) A allele is significantly associated with an increased risk of CKD. Individuals carrying the AA genotype showed a 2.19-fold higher risk, while A allele carriers had a 2.34-fold increased risk compared with the reference C allele. These findings suggest that the A allele is a genetic risk factor, whereas the C allele may confer a protective effect against CKD.

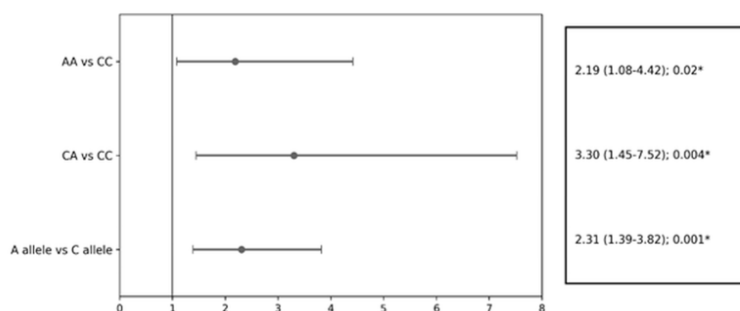


Figure 2: Forest plot for KCNA10 Genotypes

#### GENOTYPE AND ALLELE DISTRIBUTION OF SLC13A3

The SLC13A3 genotype distribution differed significantly between CKD cases and controls ( $p < 0.001$ ). The GG genotype was more frequent in controls (89.3%) than in cases (56.0%), whereas the AA genotype was more common in cases (36.0%) than in controls (10.7%). The GA genotype was detected only in cases (8.0%). Similarly, allele frequency analysis showed a significantly higher frequency of the A allele in cases (40.0%) compared to controls (10.7%), while the G allele was more frequent in controls (89.3% vs. 60.0%;  $p < 0.001$ ). These findings suggest that the A allele is associated with an increased risk of CKD, whereas the G allele may have a protective effect.

#### GENOTYPING RESULTS FOR CKD GENE SNP RS6066043 BY TETRA ARMS-PCR

The polymorphism was performed using the Tetra Amplification Refractory Mutation System-Polymerase Chain Reaction (Tetra ARMS-PCR) with allele-specific inner and outer primers. PCR amplification was carried out in a 20  $\mu$ L reaction mixture containing 2 $\times$  multiplex master mix, allele-specific primers, genomic DNA, and nuclease-free water. The PCR conditions consisted of an initial denaturation at 95°C for 15 min, followed by 32 cycles of 95°C for 30 s, 68°C for 1 min, and 72°C for 1 min, with a final extension at 72°C for 5 min. PCR products were analyzed by agarose gel electrophoresis, yielding fragment sizes of 116 bp (G allele), 101 bp (A allele), and 162 bp (outer control fragment) for genotype determination.

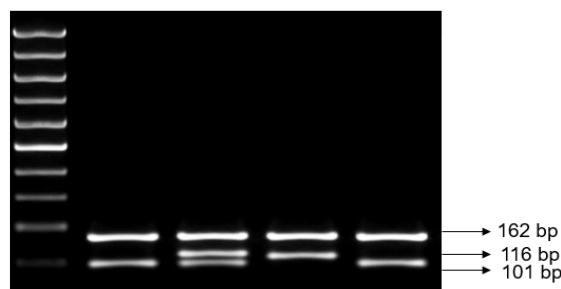


Figure : 3 Visualization of SLC13A3 (rs6066043)

### LOGISTIC REGRESSION ANALYSIS OF CKD VARIANTS – (SLC13A-rs6066043)

| Model             | Genotype / Allele | Cases n (%) | Controls n (%) | Odds Ratio (95% CI) | p-value |
|-------------------|-------------------|-------------|----------------|---------------------|---------|
| <b>Codominant</b> | GG                | 42 (56.0%)  | 67 (89.3%)     | Reference           | <0.001* |
|                   | GA                | 6(8.0%)     | 0 (0%)         | Not estimated       |         |
|                   | AA                | 27 (36.0%)  | 8 (10.7%)      | 5.39 (2.29–12.67)   |         |
| <b>Dominant</b>   | GG                | 42 (56.0%)  | 67 (89.3%)     | Reference           | <0.001* |
|                   | GA + AA           | 33 (44.0%)  | 8 (10.7%)      | 6.58 (2.89–14.98)   |         |
| <b>Recessive</b>  | GG + GA           | 48 (64.0%)  | 67 (89.3%)     | Reference           | <0.001* |
|                   | AA                | 27 (36.0%)  | 8 (10.7%)      | 4.71 (2.05–10.82)   |         |
| <b>Allelic</b>    | G                 | 90 (60.0%)  | 134 (89.3%)    | Reference           | <0.001* |
|                   | A                 | 60 (40.0%)  | 16 (10.7%)     | 5.58(3.09–10.07)    |         |

Table 3: Logistic regression analysis of CKD variants – (SLC13A-rs6066043)

Logistic regression analysis showed a significant association between the SLC13A3 (rs6066043) polymorphism and CKD. Individuals carrying the GA + AA genotype had a 6.58-fold higher risk of CKD under the dominant model (OR = 6.58, 95% CI: 2.89–14.98;  $p < 0.001$ ), while the AA genotype was associated with a 5.39-fold increased risk compared with the GG genotype (OR = 5.39, 95% CI: 2.29–12.67;  $p < 0.001$ ). Allelic analysis further demonstrated that the A allele conferred a 5.58-fold higher risk of CKD than the G allele (OR = 5.58, 95% CI: 3.09–10.07;  $p < 0.001$ ), indicating that the

A allele is a strong independent genetic risk factor for CKD

#### Association Analysis of SLC13A-rs6066043

The forest plot demonstrates a significant association between the SLC13A3 (rs6066043) A allele and CKD risk. The AA genotype was associated with a 5.39-fold increased risk, while the A allele conferred a 5.58-fold higher risk compared with the G allele ( $p < 0.001$ ). These findings indicate that the A allele is a strong genetic risk factor, whereas the G allele may have a protective role against CKD.

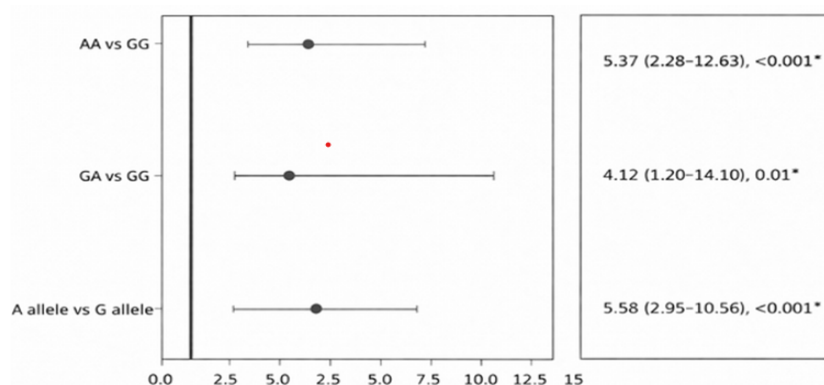


Figure : 4 Forest plot for SLC13A3 Genotypes

### Comparison of Renal Function Parameters According to KCNA10 (rs34970857) Allele Status in CKD Patients

| Parameter                                | C            | A            | p-value      |
|------------------------------------------|--------------|--------------|--------------|
| <b>Creatinine (mg/dL)</b>                | 6.39 ± 1.61  | 6.50 ± 2.24  | <b>0.81</b>  |
| <b>BUN (mg/dL)</b>                       | 70.36 ± 7.11 | 72.19 ± 9.30 | <b>0.34</b>  |
| <b>eGFR ( mL/min/1.73 m<sup>2</sup>)</b> | 20.70 ± 4.89 | 18.06 ± 3.99 | <b>0.02*</b> |
| <b>uPCR (mg/mg)</b>                      | 3.90 ± 1.40  | 3.95 ± 1.39  | <b>0.88</b>  |

TABLE 4: Association of KCNA10 Alleles with Renal Parameters Among Cases

Comparison of renal parameters between KCNA10 allele groups showed that eGFR was significantly lower in A allele carriers than C allele carriers ( $18.06 \pm 3.99$  vs.  $20.70 \pm 4.89$  mL/min/1.73 m<sup>2</sup>;  $p = 0.02$ ), indicating poorer renal function. No significant differences were

observed in serum creatinine, BUN, or uPCR between the two groups ( $p > 0.05$ ). These findings suggest that the A allele is associated with reduced kidney function in CKD patients.

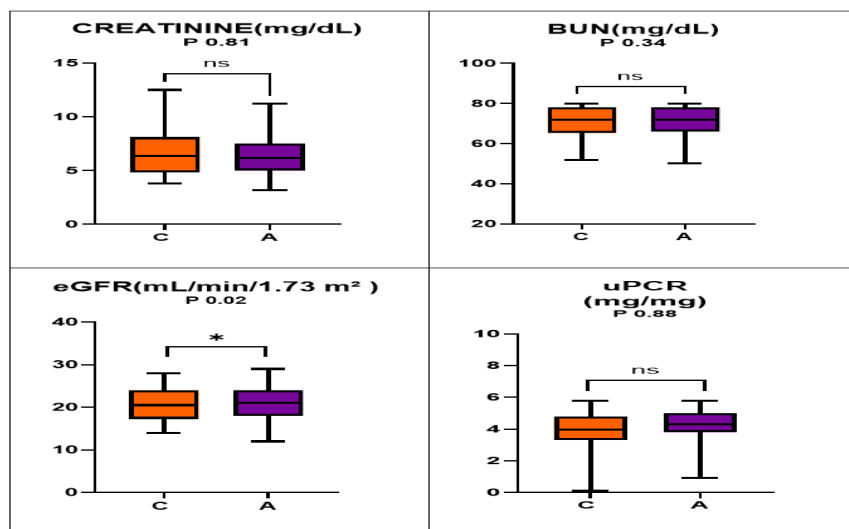


Figure : 5 Association of KCNA10 Alleles with Renal Parameters Among Cases

### Comparison of Renal Function Parameters According to SLC13A3 (rs6066043) Allele Status in CKD Patients

| Parameter                                | G            | A            | p-value           |
|------------------------------------------|--------------|--------------|-------------------|
| <b>Creatinine (mg/dL)</b>                | 6.03 ± 1.65  | 7.08 ± 2.09  | <b>0.02*</b>      |
| <b>BUN (mg/dL)</b>                       | 70.11 ± 8.13 | 78.67 ± 8.07 | <b>&lt;0.001*</b> |
| <b>eGFR ( mL/min/1.73 m<sup>2</sup>)</b> | 20.89 ± 3.90 | 16.82 ± 4.48 | <b>&lt;0.001*</b> |
| <b>uPCR (mg/mg)</b>                      | 3.70 ± 1.69  | 4.17 ± 1.01  | <b>0.15</b>       |

TABLE 5: Association of SLC13A3 Alleles with Renal Parameters Among Cases

Comparison of renal parameters between SLC13A3 allele groups showed that A allele carriers had significantly higher serum creatinine ( $7.08 \pm 2.09$  vs.  $6.03 \pm 1.65$  mg/dL;  $p = 0.02$ ) and BUN ( $78.67 \pm 8.07$  vs.  $70.11 \pm 8.13$  mg/dL;  $p < 0.001$ ), along with a significantly lower eGFR

( $16.82 \pm 4.48$  vs.  $20.89 \pm 3.90$  mL/min/1.73 m<sup>2</sup>;  $p < 0.001$ ) compared to G allele carriers. No significant difference was observed in uPCR ( $p = 0.15$ ). These findings suggest that the A allele is associated with more severe renal dysfunction in CKD patients.

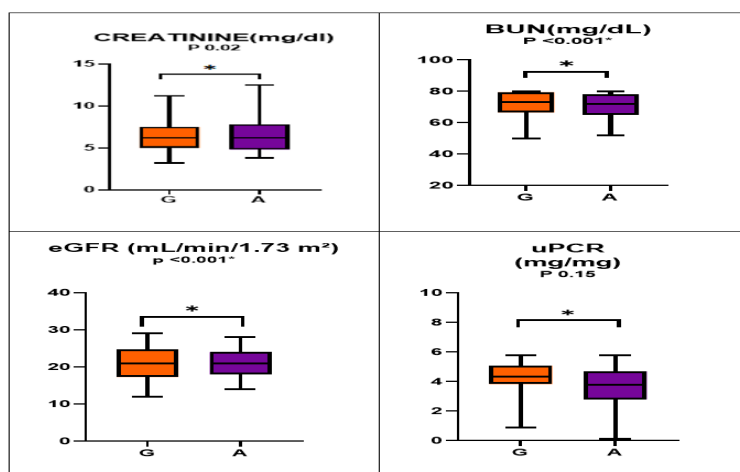


Figure : 6 Association of SLC13A3 Alleles with Renal Parameters Among Cases

#### PEARSON CORRELATION ANALYSIS OF RENAL AND BIOCHEMICAL PARAMETERS IN CKD CASES :

The correlation analysis demonstrated significant relationships among renal and biochemical parameters. eGFR showed strong negative correlations with creatinine, BUN, uPCR, HbA1c, and phosphate, and a

positive correlation with calcium, indicating that declining kidney function is associated with worsening metabolic parameters. Creatinine and BUN showed strong positive correlations with each other and with uPCR and phosphate, reflecting worsening renal impairment.

m2

| Variables                                   | eGFR<br>(mL/min/1.73m <sup>2</sup> ) | Creatinine<br>(mg/dL) | BUN<br>(mg/dL)      | uPCR<br>(mg/mg)     | HbA1c<br>(%)        | Calcium<br>(mg/dL)  | Phosphate<br>(mg/dL) |
|---------------------------------------------|--------------------------------------|-----------------------|---------------------|---------------------|---------------------|---------------------|----------------------|
| <b>eGFR</b><br>(mL/min/1.73m <sup>2</sup> ) | 1                                    | -0.82**<br>(<0.001)   | -0.76**<br>(<0.001) | -0.65**<br>(<0.001) | -0.48**<br>(<0.001) | +0.51**<br>(<0.001) | -0.58**<br>(<0.001)  |
| <b>Creatinine</b><br>(mg/dL)                | -0.82** (<0.001)                     | 1                     | +0.72**<br>(<0.001) | +0.61**<br>(<0.001) | +0.39**<br>(0.001)  | -0.44**<br>(<0.001) | +0.53**<br>(<0.001)  |
| <b>BUN</b><br>(mg/dL)                       | -0.76** (<0.001)                     | +0.72**<br>(<0.001)   | 1                   | +0.58**<br>(<0.001) | +0.36**<br>(0.003)  | -0.41**<br>(<0.001) | +0.49**<br>(<0.001)  |
| <b>uPCR</b><br>(mg/mg)                      | -0.65** (<0.001)                     | +0.61**<br>(<0.001)   | +0.58**<br>(<0.001) | 1                   | +0.42**<br>(<0.001) | -0.35**<br>(0.004)  | +0.46**<br>(<0.001)  |
| <b>HbA1c</b><br>(%)                         | -0.48** (<0.001)                     | +0.39**<br>(0.001)    | +0.36**<br>(0.003)  | +0.42**<br>(<0.001) | 1                   | -0.28*<br>(0.015)   | +0.33*<br>(0.006)    |
| <b>Calcium</b><br>(mg/dL)                   | +0.51** (<0.001)                     | -0.44**<br>(<0.001)   | -0.41**<br>(<0.001) | -0.35**<br>(0.004)  | -0.28*<br>(0.015)   | 1                   | -0.52**<br>(<0.001)  |
| <b>Phosphate</b><br>(mg/dL)                 | -0.58** (<0.001)                     | +0.53**<br>(<0.001)   | +0.49**<br>(<0.001) | +0.46**<br>(<0.001) | +0.33*<br>(0.006)   | -0.52**<br>(<0.001) | 1                    |

TABLE 6: Pearson Correlation Matrix of Renal and Biochemical Parameters (Cases)

HbA1c showed moderate positive correlations with renal dysfunction markers, suggesting a link between poor glycemic control and kidney damage. Calcium showed negative correlations with most parameters, while phosphate showed positive correlations, highlighting inverse mineral balance. Overall, the findings indicate interdependence between renal dysfunction, glycemic status, and metabolic disturbances.

## DISCUSSION

The present study demonstrated significant biochemical and genetic differences between CKD patients and healthy controls, highlighting the multifactorial nature of CKD. Age distribution was comparable between groups, while a higher proportion of males among CKD patients suggested increased susceptibility, consistent with previous studies [11].

CKD patients exhibited significantly elevated serum creatinine, BUN, uPCR, and HbA1c levels, along with reduced eGFR, confirming impaired renal function and poor glycemic control. Dyslipidemia, hypoalbuminemia, hypocalcemia, hyperphosphatemia, and elevated uric acid further reflected metabolic disturbances associated with CKD progression [12–23].

Genetic analysis revealed significant associations of KCNA10 (rs34970857) and SLC13A3 (rs6066043) polymorphisms with CKD. The A allele and A allele-containing genotypes were significantly more frequent in CKD patients and were associated with increased disease risk. Carriers of the A allele also exhibited poorer renal function, particularly lower eGFR, indicating that these polymorphisms may influence both CKD susceptibility and severity [24–29].

Correlation analysis showed strong associations between declining eGFR and worsening renal, glycemic, and metabolic parameters, emphasizing the interconnected mechanisms involved in CKD progression. The Hardy–Weinberg equilibrium observed in controls further supported the reliability of the genetic findings. Overall, the study suggests that KCNA10 and SLC13A3 polymorphisms, together with biochemical abnormalities, may serve as potential biomarkers for early identification and risk assessment of CKD [30].

## CONCLUSION

This study demonstrated that chronic kidney disease (CKD) is associated with significant renal dysfunction, metabolic abnormalities, and genetic susceptibility. CKD patients showed impaired renal function, poor glycemic control, dyslipidemia, altered protein profile, and disturbances in mineral metabolism. Furthermore, polymorphisms in the KCNA10 (rs34970857) and SLC13A3 (rs6066043) genes, particularly the A allele, were significantly associated with increased CKD risk and reduced renal function. These findings suggest that

combining biochemical markers with genetic screening may improve early detection, risk stratification, and personalized management of CKD. Further studies involving larger and more diverse populations are required to validate these findings and explore the underlying molecular mechanisms.

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