Health, Medicine and Therapeutics
ISSN Print: 3079-5079
ISSN Online: 3079-5087
https://doi.org/10.63313/hmt.9042

MS4A2 rs569108 and Diabetic Kidney Disease in Type 2 Diabetes

Xinhuan An. Fang Wang and Ying Lu
Department of Endocrinology, Zhongshan People's Hospital, Zhongshan, China
Email: axh1998@sina.com

How to cite this paper: An, X., Wang, F., & Lu, Y. (2026). MS4A2 rs569108 and Diabetic Kidney Disease in Type 2 Diabetes. Health, Medicine and Therapeutics, 2(2), 115–125. ISSN Print: 3079-5079, ISSN Online: 3079-5087.
https://doi.org/10.63313/hmt.9042
Published: 2026-09-30

Copyright © 2026 by author(s) and Erytis Publishing Limited.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/

Abstract

Objective: To summarize project 20231A020023 by evaluating MS4A2 (FcεRIβ) rs569108 in relation to diabetic kidney disease (DKD), albuminuria and renal function. Methods: Unrelated patients with type 2 diabetes mellitus (T2DM), diagnosed according to the 1999 WHO criteria, were studied after excluding other causes of proteinuria and renal disease. UACR defined dn0 (<30), dn1 (30–<300) and dn2 (≥300 mg/g). Adult eGFR was calculated using the 2021 CKD-EPI creatinine equation. The analytical DKD phenotype was UACR ≥30 mg/g or eGFR <60 mL/min/1.73 m^2. Genotype distributions and multivariable regression were evaluated, with 40 separate healthy controls. Results: Genotype/UACR analyses included 499 diabetic records (dn0/dn1/dn2: 332/128/39). Among 497 records with adult eGFR, 44 had reduced eGFR, 196 met the analytical DKD definition and 301 did not. The adjusted per-C-allele OR was 0.95 (95% CI 0.71–1.27; P=0.737) for DKD, 1.27 (95% CI 0.77–2.10; P=0.351) for reduced eGFR, and 0.85 (95% CI 0.63–1.15; P=0.297) for albuminuria. Overall genotype distributions did not differ across dn0/dn1/dn2 (P=0.275). An exploratory dn2-versus-dn0 association did not remain significant after multiplicity adjustment. Conclusions: The available data do not demonstrate an independent association of rs569108 with DKD or reduced renal function. Cross-sectional measurement, the small reduced-eGFR subgroup and residual data limitations restrict causal and prognostic interpretation.

Keywords

MS4A2; rs569108; FcεRIβ; Diabetic Kidney Disease; Albuminuria; Estimated Glomerular Filtration Rate

1. Introduction

Diabetic kidney disease (DKD) is a major microvascular complication of diabetes. Its clinical assessment combines albuminuria, glomerular filtration and evidence of persistence, because a single abnormal measurement does not establish chronic kidney disease [1]. Genetic susceptibility and inflammatory pathways provide complementary explanations for heterogeneity in kidney involvement among people with type 2 diabetes mellitus (T2DM) [2–4]. A candidate variant therefore

requires direct clinical evaluation rather than inference from pathway plausibility alone.

The high-affinity IgE receptor is relevant to inflammatory-cell signaling. Sur et al. reported FcER1-related transcriptional and protein findings in human DKD, including FCER1G expression [5]. That evidence concerns receptor biology and does not establish an association for the β-chain gene MS4A2. The rs569108 variant, historically described as E237G, has been investigated in allergic phenotypes [6,7]. Whether it is associated with albuminuria in T2DM remains a distinct empirical question.

This original research article summarizes the Zhongshan Health Bureau project "Association of FcER1β rs569108 polymorphism with diabetic kidney disease" (20231A020023). The project proposed Sanger genotyping, renal biomarker comparisons and multivariable association analysis. We assessed whether rs569108 genotype was associated with UACR-defined albuminuria in T2DM and used a separate healthy control group to place the diabetic genotype distribution in context. The study is a cross-sectional project summary, and does not measure incident DKD or longitudinal progression.

2. Materials and Methods

2.1. Study population and sample identification

De-identified clinical and genetic records were supplied for the project at the Department of Endocrinology, Zhongshan People's Hospital, China. The clinical dataset contained 530 diabetic records numbered 1–530. The project team designated all unsuffixed genotype labels as diabetic samples and all labels ending in "-1" as independent healthy controls. Thus, 501 and 501-1 identify different participants; the suffix does not indicate a repeat assay. Diabetic records were linked by identical identifiers without stripping suffixes. The healthy controls had genotype information only and were excluded from analyses requiring UACR or clinical covariates.

The study enrolled patients with DKD and patients with T2DM without DKD. T2DM was diagnosed according to the 1999 World Health Organization diagnostic criteria [10]. Participants were unrelated to one another. Other factors capable of causing proteinuria and other renal diseases were excluded before renal phenotype classification. These eligibility conditions were confirmed by the project team. The administrative project period was January 2023 to December 2025; actual recruitment dates were not specified. Healthy controls remained a separate, genotype-only comparison group.

2.2. Genotyping

The protocol specified extraction of genomic DNA from peripheral-blood leukocytes, PCR amplification and Sanger sequencing. The primer sequences were forward

5′-CAGGTTCCAGAGCATCGTG-3′ and reverse 5′-CTTATAAATCAATGGGAGGAAACA-3′. This analysis used the reported rs569108 calls. Chromatograms, assay batches, blinding, replicate testing and sequencing-quality metrics were unavailable; therefore, the protocol does not independently document assay execution for every sample. The genetic file is a single-SNP dataset rather than a genome-wide dataset.

TT, TC and CC were retained as recorded, and NN indicated a missing call. The T/C labels are complementary to the A/G notation reported for E237G [6]; biological strand assignment requires laboratory confirmation. Genotypic models compared TC and CC with TT. Additive models coded recorded C-allele dosage as 0, 1 or 2, and dominant models compared TC+CC with TT. Healthy control labels were neither substituted for diabetic genotypes nor treated as repeated samples.

2.3. Albuminuria groups and clinical variables

UACR was expressed in mg/g. The project groups dn0, dn1 and dn2 denoted UACR <30, 30 to <300 and ≥300 mg/g, respectively, corresponding to no increased albuminuria, microalbuminuria and macroalbuminuria. These align with A1, A2 and A3 categories [1]. Renal function was classified as reduced eGFR (<60) or normal/preserved eGFR (≥60 mL/min/1.73 m^2). Within the confirmed eligibility framework, the operational DKD phenotype for regression was UACR ≥30 mg/g or eGFR <60; the non-DKD reference required both UACR <30 and eGFR ≥60. Thus, dn0 was not automatically equated with absence of DKD. This cross-sectional classification does not independently document persistence for at least three months. Serial UACR, serial renal function and blood/urine β2-microglobulin were unavailable.

Serum creatinine was recorded in μmol/L and divided by 88.4 to obtain mg/dL. For participants aged ≥18 years, eGFR was calculated using the race-free 2021 CKD-EPI creatinine equation [11,12]: 142 × min(Scr/κ,1)^α × max(Scr/κ,1)^−1.200 × 0.9938^age × 1.012 (if female), where κ is 0.7 for women and 0.9 for men, and α is −0.241 and −0.302, respectively. Results are indexed to 1.73 m^2. One 16-year-old participant was retained for albuminuria analysis but excluded from adult-equation renal analyses; one other record lacked creatinine. No pediatric estimate was substituted. The supplied “eGFR (mL/min)” column matched unindexed Cockcroft–Gault creatinine clearance to rounding precision in all 525 available records. It was preserved as source information but not substituted for indexed eGFR. Creatinine assay traceability was not documented.

Clinical covariates were diabetes duration, sex, age, height, weight, blood pressure, waist, hip, fasting glucose and HbA1c. BMI was calculated as kg/m^2 and waist-to-hip ratio as waist divided by hip. Delimited blood pressures were separated into systolic and diastolic values. Eleven undelimited five-digit pressure entries and one HbA1c value of 0.2% were treated as missing in adjusted models because their interpretation was uncertain. Four weights and one additional HbA1c value were

unavailable. No missing covariate was imputed. Empty treatment fields were not interpreted as absence of treatment.

2.4. Statistical Analysis

Continuous variables were summarized as medians and interquartile ranges and compared across dn0/dn1/dn2 using Kruskal–Wallis tests; sex was compared using a chi-square test. Genotype distributions were compared using conditional exact contingency-table tests with 99,999 Monte Carlo samples (seed 20260928). Comparisons comprised the three diabetic groups, dn0 versus dn1+dn2, all four groups including healthy controls, and T2DM versus healthy controls. Secondary healthy-control comparisons used Benjamini–Hochberg adjustment across four tests. Hardy–Weinberg equilibrium (HWE) was assessed by a conditional exact test [8], without genotype exclusions based on HWE.

Logistic regression estimated odds ratios (ORs) and 95% confidence intervals (CIs) for the operational DKD phenotype, albuminuria (dn1+dn2 versus dn0), and reduced eGFR. Genotypic models used TC and CC indicators with TT as reference; joint genotype effects were assessed using two-degree-of-freedom likelihood-ratio tests. Additive and dominant models evaluated per-C-allele and TC+CC-versus-TT associations. Full models adjusted for age, sex, diabetes duration, BMI, systolic pressure and HbA1c, selected for clinical relevance without stepwise selection. Creatinine and UACR were not added as adjustment variables for outcomes they define. Complete-case analysis was used. Healthy-control comparisons remained unadjusted because clinical covariates were unavailable.

Natural-log UACR and continuous eGFR were evaluated using linear regression with HC3 robust standard errors. Exponentiated log-UACR coefficients represent conditional geometric mean ratios; eGFR coefficients represent differences in mL/min/1.73 m^2. Spearman correlations of C-allele dosage with 11 clinical traits, including creatinine and eGFR, used Benjamini–Hochberg false-discovery-rate adjustment. Three exploratory additive comparisons (dn1 versus dn0, dn2 versus dn0 and dn2 versus dn1) were separately adjusted for multiplicity. Renal-function regression was restricted to adults with creatinine and an evaluable eGFR. A separate analysis compared reduced with preserved eGFR within the DKD group, as specified in the project framework.

All tests were two-sided with a nominal significance threshold of 0.05. Exploratory subgroup findings were interpreted together with their multiplicity-adjusted q values and confidence intervals. Statistical analysis used Python, pandas, SciPy and statsmodels. Reporting followed relevant STREGA recommendations [9].

3. Results

3.1. Study Groups and Clinical Characteristics

The genotype file contained 504 diabetic and 40 independent healthy control labels.

Of 530 clinical records, 26 lacked a genotype label and five had NN calls, leaving 499 records for genotype/UACR analyses: 332 dn0, 128 dn1 and 39 dn2. There were 229 males (45.9%). All 40 healthy-control genotypes were usable. Adult eGFR was available for 497 genotyped records; one record lacked creatinine and one participant was aged 16 years. The adjusted albuminuria model included 482 records and 165 events. Renal models included 480 complete cases, with 193 DKD and 43 reduced-eGFR events (Figure 1; Table 1).

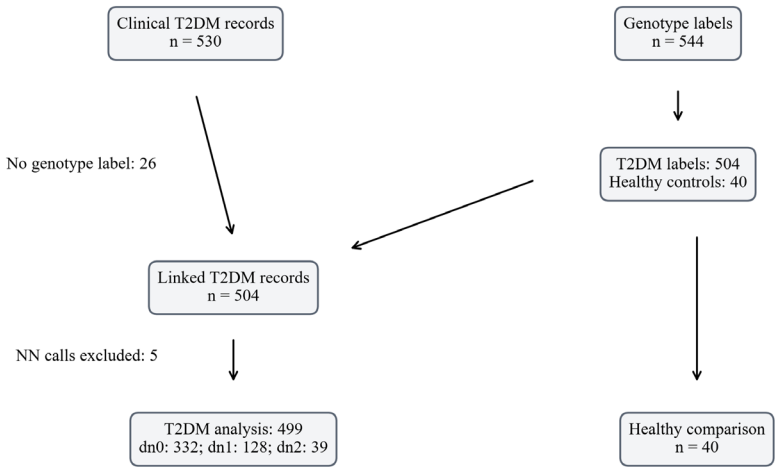


Figure 1. Clinical and genotype linkage. Healthy controls are independent participants. Of the 499 records in albuminuria analyses, 497 had adult CKD-EPI eGFR: 196 met the operational DKD definition and 301 did not. One record lacked creatinine and one participant was aged 16 years.

Table 1. Clinical characteristics by albuminuria category

Characteristic	dn0 n=332	dn1 n=128	dn2 n=39	P
Age, years	61.0 [49.0–69.0]	60.0 [45.8–69.0]	58.0 [43.5–64.5]	0.493
Male, n (%)	145 (43.7)	62 (48.4)	22 (56.4)	0.256
Diabetes duration, years	5.0 [2.0–10.0]	4.0 [2.0–8.0]	6.0 [3.5–10.0]	0.347
BMI, kg/m^2	23.6 [21.3–25.7]	23.9 [21.7–26.0]	24.1 [21.9–25.7]	0.538
Systolic BP, mmHg	139.0 [125.2–157.0]	145.0 [126.5–160.5]	141.0 [127.5–150.5]	0.320
Diastolic BP, mmHg	82.0 [72.0–90.0]	84.0 [74.0–92.0]	87.0 [75.5–93.5]	0.236
Fasting glucose, mmol/L	7.8 [6.5–10.0]	7.5 [6.5–10.0]	7.6 [6.5–8.9]	0.779
HbA1c, %	8.1 [7.0–10.2]	8.1 [7.0–10.1]	7.7 [7.0–9.0]	0.502
UACR, mg/g	14.2 [10.3–20.3]	68.8 [55.1–122.9]	519.2 [390.9–800.8]	<0.001
Waist-to-hip ratio	0.93 [0.89–0.98]	0.94 [0.90–0.99]	0.93 [0.90–0.98]	0.522
Serum creatinine, μmol/L	74.0 [64.5–85.0]	76.0 [65.0–87.0]	74.0 [65.0–87.0]	0.696

eGFR, mL/min/1.73 m^2	89.5 [73.7–101.3]	87.7 [71.7–101.8]	91.8 [78.5–105.5]	0.518

Values are median [Q1–Q3] unless indicated otherwise. Available observations are listed in Table S1. UACR differences follow directly from the grouping rule. Clinical covariates for healthy controls were unavailable.

3.2. Genotype distribution and healthy controls

Among diabetic records, 284 (56.9%) were TT, 176 (35.3%) TC and 39 (7.8%) CC; the C-allele frequency was 25.5%. Healthy controls comprised 21 TT, 17 TC and 2 CC genotypes, with a C-allele frequency of 26.3%. The dn0, dn1 and dn2 C-allele frequencies were 26.4%, 26.2% and 15.4%, respectively (Table 2; Figure 2). The overall three-diabetic-group genotype test was not significant (P=0.275), nor was dn0 versus dn1+dn2 (P=0.663). The four-group comparison including healthy controls yielded P=0.419, and T2DM versus healthy controls yielded P=0.661. Secondary control comparisons remained nonsignificant after false-discovery-rate adjustment (Table S4).

The unadjusted per-C-allele OR for T2DM versus healthy status was 0.96 (95% CI 0.58–1.59; P=0.878). This secondary comparison was not adjusted for age, sex or other clinical variables. Exact HWE P values were 0.700 in healthy controls, 0.125 in T2DM overall, 0.260 in dn0, 0.646 in dn1 and 0.196 in dn2; none indicated a nominal departure. No sample was removed because of HWE.

Table 2. Genotype and allele distributions

Group	n	TT n (%)	TC n (%)	CC n (%)	C allele %	HWE P
Healthy	40	21 (52.5)	17 (42.5)	2 (5.0)	26.25	0.700
T2DM	499	284 (56.9)	176 (35.3)	39 (7.8)	25.45	0.125
dn0	332	184 (55.4)	121 (36.4)	27 (8.1)	26.36	0.260
dn1	128	71 (55.5)	47 (36.7)	10 (7.8)	26.17	0.646
dn2	39	29 (74.4)	8 (20.5)	2 (5.1)	15.38	0.196

T2DM is the pooled dn0/dn1/dn2 cohort and is not an additional independent group. Genotype-distribution P values: dn0/dn1/dn2, 0.275; healthy/dn0/dn1/dn2, 0.419; T2DM versus healthy, 0.661. HWE uses conditional exact tests and was not an exclusion criterion.

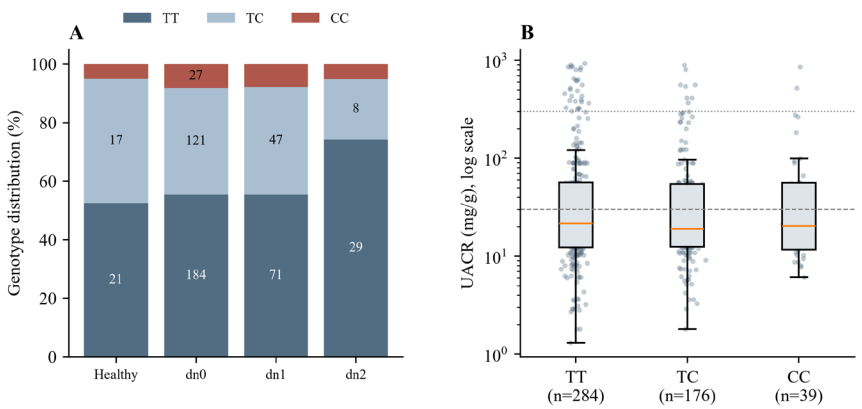


Figure 2. Genotypes and UACR. (A) Genotype percentages in healthy controls and dn0/dn1/dn2; internal labels are counts where space permits. (B) Diabetic UACR by genotype on a logarithmic scale. Boxes show medians and quartiles, whiskers extend to 1.5 interquartile ranges, and points show individual observations. Horizontal lines mark 30 and

300 mg/g.

3.3. Multivariable associations with albuminuria

In the fully adjusted genotypic model, TC versus TT had an OR of 0.79 (95% CI 0.53–1.20; P=0.271), and CC versus TT had an OR of 0.81 (95% CI 0.39–1.68; P=0.568). The joint genotype likelihood-ratio test yielded P=0.510. The adjusted additive OR per C allele was 0.85 (95% CI 0.63–1.15; P=0.297), and the dominant OR for TC+CC versus TT was 0.80 (95% CI 0.54–1.17; P=0.248) (Table 3; Figure 3). These estimates did not demonstrate an association with UACR ≥30 mg/g. All fitted logistic models converged, and variance inflation factors in the additive model were below 1.11.

The adjusted geometric mean UACR ratio per C allele was 0.93 (95% CI 0.78–1.11; P=0.411). The Spearman correlation with UACR was −0.044 (P=0.325). In exploratory models, the adjusted dn2-versus-dn0 OR was 0.52 (95% CI 0.28–0.99; P=0.046). Although the nominal P value was below 0.05, the three-comparison false-discovery-rate q value was 0.111, so this was not considered a multiplicity-adjusted significant association. The dn1-versus-dn0 and dn2-versus-dn1 comparisons were also nonsignificant after adjustment (Table S5).

Table 3. Logistic regression for dn1+dn2 versus dn0

Model	n/events	OR (95% CI)	P
TC versus TT, unadjusted	499/167	0.84 (0.56–1.25)	0.383
CC versus TT, unadjusted	499/167	0.82 (0.40–1.68)	0.585
TC versus TT, adjusted	482/165	0.79 (0.53–1.20)	0.271
CC versus TT, adjusted	482/165	0.81 (0.39–1.68)	0.568
Per C allele, unadjusted	499/167	0.87 (0.65–1.17)	0.372
Per C allele, age/sex	499/167	0.87 (0.65–1.17)	0.353
Per C allele, adjusted	482/165	0.85 (0.63–1.15)	0.297
TC+CC versus TT, adjusted	482/165	0.80 (0.54–1.17)	0.248

Full adjustment: age, sex, diabetes duration, BMI, systolic BP and HbA1c. The joint two-degree-of-freedom genotype likelihood-ratio P value is 0.510. Individual CIs and P values use Wald estimates.

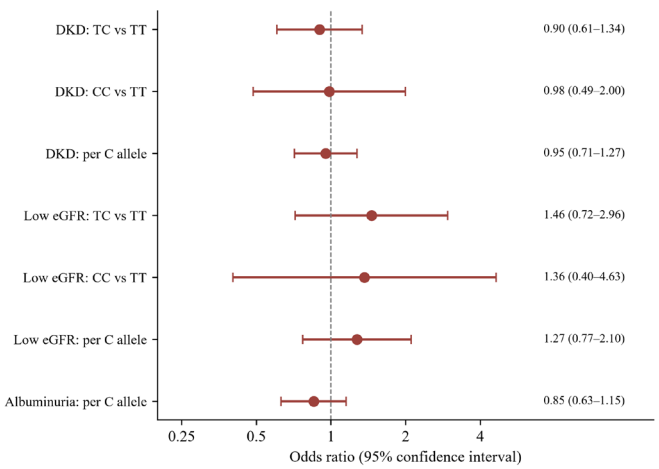


Figure 3. Adjusted genetic associations with DKD, reduced eGFR and albuminuria. Points and lines show ORs and 95% CIs. All models adjust for age, sex, duration, BMI, systolic BP and HbA1c. DKD is the combined UACR/eGFR phenotype; low eGFR is <60 mL/min/1.73 m^2. The vertical line marks OR=1.

3.4. Renal function and the DKD phenotype

Among 497 evaluable adult records, 44 had eGFR <60 and 453 had eGFR ≥60 mL/min/1.73 m^2. Reduced eGFR occurred in 30/331 dn0, 10/127 dn1 and 4/39 dn2 records. Combining UACR and eGFR classified 196 records as the DKD phenotype and 301 as non-DKD. The 30 dn0 records with reduced eGFR illustrate why albuminuria-only grouping does not capture all kidney involvement. Genotype distributions were not significantly different for DKD versus non-DKD (exact P=0.937) or reduced versus preserved eGFR (P=0.579; Table 4).

Table 4. Genotypes by DKD phenotype and renal-function group

Group	n	TT, n (%)	TC, n (%)	CC, n (%)	C allele %
Non-DKD	301	170 (56.5)	108 (35.9)	23 (7.6)	25.6
DKD	196	114 (58.2)	67 (34.2)	15 (7.7)	24.7
eGFR >=60	453	262 (57.8)	157 (34.7)	34 (7.5)	24.8
eGFR <60	44	22 (50.0)	18 (40.9)	4 (9.1)	29.5

The two classifications describe the same 497 records, not independent samples. eGFR units: mL/min/1.73 m^2. Exact genotype-distribution P values: DKD versus non-DKD, 0.937; eGFR <60 versus ≥60, 0.579.

The fully adjusted per-C-allele OR was 0.95 (95% CI 0.71–1.27; P=0.737) for DKD and 1.27 (95% CI 0.77–2.10; P=0.351) for reduced eGFR (Table 5; Figure 3). Categorical genotype tests were also nonsignificant (joint P=0.872 for DKD and P=0.564 for reduced eGFR). The adjusted continuous-eGFR difference per C allele was -0.62 mL/min/1.73 m^2 (95% CI -2.86–1.61; P=0.583). Neither creatinine nor eGFR showed a significant dosage correlation after false-discovery-rate adjustment (Table S2).

Within the 196 DKD records, 44 had reduced eGFR and 152 had preserved eGFR. TT/TC/CC counts were 22/18/4 and 92/49/11, respectively (exact genotype-distribution P=0.422). Restricting the regression to DKD gave an adjusted per-C-allele OR of 1.68 (95% CI 0.92–3.09; P=0.094) for reduced versus preserved eGFR (n=193). This within-DKD analysis also did not demonstrate a significant association.

Table 5. Regression for DKD and reduced eGFR

Outcome and model	n/events	OR (95% CI)	P
DKD, per C, unadjusted	497/196	0.96 (0.72–1.27)	0.774
DKD, per C, adjusted	480/193	0.95 (0.71–1.27)	0.737
DKD, TC vs TT	480/193	0.90 (0.61–1.34)	0.603
DKD, CC vs TT	480/193	0.98 (0.49–2.00)	0.965
DKD, TC+CC vs TT	480/193	0.92 (0.63–1.33)	0.640
Low eGFR, per C, unadjusted	497/44	1.25 (0.78–1.99)	0.348
Low eGFR, per C, adjusted	480/43	1.27 (0.77–2.10)	0.351
Low eGFR, TC vs TT	480/43	1.46 (0.72–2.96)	0.297
Low eGFR, CC vs TT	480/43	1.36 (0.40–4.63)	0.618

Low eGFR, TC+CC vs TT	480/43	1.44 (0.74–2.82)	0.287
Within DKD, low eGFR per C	193/43	1.68 (0.92–3.09)	0.094

Except rows explicitly marked unadjusted, models adjust for age, sex, duration, BMI, systolic BP and HbA1c. Per C means per recorded C allele. DKD is UACR ≥30 mg/g or adult eGFR <60 mL/min/1.73 m^2; reference requires both normal UACR and preserved eGFR.

4. Discussion

This project summary found no statistically significant independent association of MS4A2 rs569108 with the combined DKD phenotype, albuminuria or reduced eGFR. Incorporating creatinine extended the project beyond albuminuria-only classification and identified 30 dn0 records with reduced filtration. The separate healthy-control comparison likewise did not demonstrate a genotype-distribution difference. The DKD comparison addresses kidney involvement within T2DM, while the healthy-control comparison addresses sampled diabetes status; these are distinct questions.

The biological rationale remains relevant but requires careful interpretation. FcER1-related inflammatory signaling has been implicated in human DKD, with prior work emphasizing FCER1G-associated findings [5]. That receptor-pathway evidence is not direct evidence for a susceptibility effect of the MS4A2 β-chain variant. Likewise, associations of rs569108 with allergic phenotypes [6,7] do not establish a kidney-disease mechanism. This study had no receptor-expression, IgE, immune-cell or functional data with which to connect genotype to downstream inflammation or fibrosis. It therefore tests a clinical genetic association rather than a causal molecular pathway.

The lower C-allele frequency in dn2 remains exploratory. The adjusted dn2-versus-dn0 comparison reached nominal significance but not significance after adjustment for the three subgroup comparisons. Only 39 records belonged to dn2, and the reduced-eGFR model contained 43 complete-case events with several adjustment variables. These relatively small event counts and wide confidence intervals limit precision. Neither a protective association nor clinical predictive utility follows from these findings. The overall nonsignificant results also do not establish equivalence or exclude smaller effects.

The confirmed WHO-based diagnosis, absence of relatedness and exclusion of other causes of proteinuria provide the clinical framework for this analysis. Nevertheless, single-time-point UACR and creatinine do not independently establish chronic persistence, and no longitudinal outcome was available. The distinction between indexed CKD-EPI eGFR and the unindexed clearance in the source spreadsheet is essential because applying the same numeric threshold to the two measures produces different classifications. Creatinine assay calibration was not documented, cystatin C was unavailable, and the adult equation was not extrapolated to the 16-year-old participant [11,12]. These limitations affect phenotype precision without changing the study's stated eligibility criteria.

Other limitations include the small healthy-control group without clinical covariates, missing blood/urine β2-microglobulin, empty treatment fields and possible selection from complete-case analysis. Unusually regular differences between paired clinical record blocks still merit source confirmation, but their cause cannot be inferred from the spreadsheet. HWE tests were nonsignificant and were not used to exclude samples. Assay documentation and independent replication would strengthen the genetic interpretation [8,9].

As a summary of project 20231A020023, this analysis now integrates genotype distributions, albuminuria strata and creatinine-based renal-function strata. The β2-microglobulin objective and longitudinal progression assessment remain unaddressed by the available measurements. The results provide a documented evaluation of the candidate variant without supporting genotype-guided DKD prediction or treatment.

5. Conclusion

Among unrelated patients with WHO-defined T2DM after exclusion of other causes of proteinuria and renal disease, MS4A2 rs569108 showed no significant independent association with the cross-sectional DKD phenotype, albuminuria or reduced eGFR. The healthy-control comparison was also nonsignificant. These findings summarize the project's available clinical genetic evidence and do not support treating rs569108 as an established DKD risk marker. Longitudinal phenotype confirmation and independent replication remain necessary.

6. Declarations

Funding: This work summarizes the Zhongshan Health Bureau project "Association of FcER1β rs569108 polymorphism with diabetic kidney disease" (20231A020023), as identified in the supplied author information. The funder's role has not been documented and must be confirmed by the authors.

Author contributions and competing interests: The supplied author order is Xinhuan An, Fang Wang and Ying Lu. Individual contributions, corresponding-author designation, competing-interest statements and approval of the manuscript require confirmation by these authors; no contribution or declaration is inferred from the author list.

Data availability: Aggregate results are provided in the tables and statistical supplement. The clinical and genetic source files are held by the project team. Any sharing of participant-level data requires the team's authorization and applicable ethics arrangements; public release is not asserted. This manuscript is a research draft pending source-data and author verification.

References

[1] Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. (2024) KDIGO

2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International, 105(Suppl 4S), S117–S314. https://doi.org/10.1016/j.kint.2023.10.018

[2] Wei, L., Xiao, Y., Li, L., et al. (2018) The Susceptibility Genes in Diabetic Nephropathy. Kidney Diseases, 4, 226–237. https://doi.org/10.1159/000492633

[3] Gu, H.F. (2019) Genetic and Epigenetic Studies in Diabetic Kidney Disease. Frontiers in Genetics, 10, 507. https://doi.org/10.3389/fgene.2019.00507

[4] Pérez-Morales, R.E., Del Pino, M.D., Valdivielso, J.M., Ortiz, A., Mora-Fernández, C. and Navarro-González, J.F. (2019) Inflammation in Diabetic Kidney Disease. Nephron, 143, 12–16. https://doi.org/10.1159/000493278

[5] Sur, S., Nguyen, M., Boada, P., Sigdel, T.K., Sollinger, H.W. and Sarwal, M.M. (2021) FcER1: A Novel Molecule Implicated in the Progression of Human Diabetic Kidney Disease. Frontiers in Immunology, 12, 769972. https://doi.org/10.3389/fimmu.2021.769972

[6] Hill, M.R. and Cookson, W.O.C.M. (1996) A New Variant of the β Subunit of the High-Affinity Receptor for Immunoglobulin E (FcεRI-β E237G): Associations with Measures of Atopy and Bronchial Hyper-Responsiveness. Human Molecular Genetics, 5, 959–962. https://doi.org/10.1093/hmg/5.7.959

[7] Hua, L., Chen, Q., Liu, Q.H., et al. (2021) Interaction between Antibiotic Use and MS4A2 Gene Polymorphism on Childhood Eczema: A Prospective Birth Cohort Study. BMC Pediatrics, 21, 314. https://doi.org/10.1186/s12887-021-02786-x

[8] Wigginton, J.E., Cutler, D.J. and Abecasis, G.R. (2005) A Note on Exact Tests of Hardy–Weinberg Equilibrium. American Journal of Human Genetics, 76, 887–893. https://doi.org/10.1086/429864

[9] Little, J., Higgins, J.P.T., Ioannidis, J.P.A., et al. (2009) Strengthening the Reporting of Genetic Association Studies (STREGA): An Extension of the STROBE Statement. European Journal of Epidemiology, 24, 37–55. https://doi.org/10.1007/s10654-008-9302-y

[10] World Health Organization. (1999) Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. Part 1: Diagnosis and Classification of Diabetes Mellitus. WHO/NCD/NCS/99.2. Geneva: WHO. https://www.paho.org/sites/default/files/WHO-Definition-Diagnoses-Classification-Diabetes-1999.pdf

[11] Inker, L.A., Eneanya, N.D., Coresh, J., et al. (2021) New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race. New England Journal of Medicine, 385, 1737–1749. https://doi.org/10.1056/NEJMoa2102953

[12] National Institute of Diabetes and Digestive and Kidney Diseases. eGFR Equations for Adults. Accessed 29 September 2026. https://www.niddk.nih.gov/research-funding/research-programs/kidney-clinical-research-epidemiology/laboratory/glomerular-filtration-rate-equations/adults