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Do gut-derived metabolites relate to changes in kidney function in adults with chronic kidney disease?

Submission date
10/11/2026

Recruitment status
No longer recruiting

Registration date
13/11/2026

Overall study status
Completed

Last Edited
11/11/2026

Condition category
Urological and Genital Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Chronic kidney disease (CKD) is a long-term condition in which the kidneys gradually lose some of their ability to filter waste products from the blood. Gut bacteria produce substances when they break down food. Some of these substances can enter the bloodstream and may be related to kidney health. This study aims to examine selected substances produced by gut bacteria in adults with CKD and investigate whether they are associated with changes in kidney function over 12 months. The study will also examine possible links with inflammation, oxidative stress and the function of the intestinal barrier.

Who can participate?
Patients aged 18 years or older with confirmed chronic kidney disease, stages G1 to G5, who are not receiving dialysis

What does the study involve?
Participants are followed for 12 months while continuing their usual medical care. No experimental treatment or study medication is assigned. Kidney function is assessed at the beginning of the study and at months 3, 6, 9 and 12. Blood samples are collected at the beginning of the study and at months 6 and 12 to measure selected substances produced by gut bacteria and other markers related to inflammation, oxidative stress and intestinal health. Urine samples are also collected for kidney-related assessments. Stool samples are used for gut microbiome assessment where available. Relevant clinical information, medication use and dietary information are recorded during follow-up.

What are the possible benefits and risks of participating?
Participants may not receive a direct personal benefit from taking part, and improvement in kidney function cannot be guaranteed. However, the information collected may improve understanding of how substances produced by gut bacteria are associated with kidney function in people with CKD and may help guide future research.
Possible risks and inconveniences include temporary pain, bruising or lightheadedness associated with blood collection, the time required for repeat visits and sample collection, and

the potential risk of loss of confidentiality. Study information is handled using participant codes and appropriate confidentiality procedures.

Where is the study run from?
Decheng District Traditional Chinese Medicine Hospital (Dezhou United Hospital) (China)

When is the study starting and how long is it expected to run for?
October 2024 to October 2026

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal investigator

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Study information

Scientific Title
Associations of gut–kidney axis microbial metabolites with 12-month renal function decline in adults with chronic kidney disease: a prospective cohort study

Study objectives
1. To characterise baseline and longitudinal profiles of selected gut microbiota-derived metabolites in adults with CKD stages G1–G5
2. To determine the associations between metabolite concentrations and the rate of renal function decline over 12 months, measured by the eGFR slope
3. To examine the statistical mediating roles of systemic inflammation, oxidative stress, and intestinal epithelial injury
4. To assess whether CKD stage and diabetes status modify the associations between metabolite concentrations and renal-function trajectories

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 01/10/2024, Institutional Review Board of Decheng District Traditional Chinese Medicine Hospital (Decheng District Traditional Chinese Medicine Hospital (Dezhou United Hospital), No. 8 Mashi Street, Decheng District, Dezhou, Shandong, 253000, China; +86 (0)534-2617779; lhyybgs@126.com), ref: IRB-KQJ482

Primary study design
Observational

Secondary study design
Prospective single-centre longitudinal cohort study with 12 months of follow-up

Study type(s)

Health condition(s) or problem(s) studied
Chronic kidney disease (CKD), specifically non-dialysis CKD stages G1–G5

Interventions
This was a prospective, single-centre, 12-month observational cohort study of adults with non-dialysis CKD stages G1–G5 attending the nephrology outpatient service. Potential participants were approached consecutively between 01/10/2024 and 31/10/2025 through clinic appointment lists and clinician referrals. Eligibility was determined using age, documented CKD duration and stage, clinical stability, dialysis and transplant history, comorbidities, recent antibiotic and probiotic/prebiotic exposure, and ability to provide written informed consent.

A total of 290 participants were enrolled. No study treatment, investigational medicinal product, device, or behavioural intervention was assigned. Participants continued usual clinical care. Study procedures consisted of scheduled clinical and renal-function assessments, blood and urine specimen collection, laboratory measurement of gut microbiota-related metabolites and host-response markers, and abstraction of relevant medication, dietary, gastrointestinal symptom, laboratory, and imaging records.

Clinical and renal-function assessments were scheduled at baseline and months 3, 6, 9, and 12. Serum creatinine was measured at these five timepoints using an enzymatic assay traceable to isotope dilution mass spectrometry (IDMS) reference materials. eGFR was calculated using the 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation. The primary outcome was the annual eGFR slope over 12 months, estimated from repeated eGFR values using a longitudinal mixed-effects model.

Fasting venous blood was collected after an 8–12-hour fast: 10 ml at baseline and 8 ml at months 6 and 12. Serum indoxyl sulfate (IS) and p-cresyl sulfate (pCS) were quantified by liquid chromatography–tandem mass spectrometry (LC-MS/MS) using isotope-labelled internal standards; trimethylamine N-oxide (TMAO) was quantified by isotope-dilution LC–MS/MS; and acetate, propionate, and butyrate were measured separately after 3-nitrophenylhydrazine derivatisation by LC–MS/MS. These six serum metabolites were assessed at baseline, month 6, and month 12.

First-morning midstream urine was collected and processed for urinary albumin and creatinine measurement; UACR was calculated as urinary albumin (mg/l) divided by urinary creatinine (g/l) and reported in mg/g. The manuscript reports baseline and month-12 UACR values. CONFIRM the actual urine collection visit schedule against the source specimen log or case-report forms before entering any additional timepoints.

Candidate mediator markers were measured at baseline, month 6, and month 12. These comprised hsCRP, IL-6, and TNF-α for systemic inflammation; malondialdehyde (MDA) and superoxide dismutase (SOD) activity for oxidative stress; and intestinal fatty acid-binding protein (I-FABP) as a marker of enterocyte injury. I-FABP was not treated as a direct functional measure of intestinal permeability.

Intervention Type
Other

Primary outcome(s)
1. Annual eGFR slope measured using annual change in estimated glomerular filtration rate (eGFR), expressed as ml/min/1.73 m^2/year. Serum creatinine is measured using an enzymatic assay traceable to IDMS reference materials. eGFR is calculated using the 2021 CKD-EPI creatinine equation. The annual slope is estimated from repeated eGFR measurements using the participant-specific time coefficient in a longitudinal mixed-effects model; a more negative slope indicates faster renal-function decline. Measured at baseline and months 3, 6, 9, and 12. The annual slope is estimated over the 12-month follow-up period.

Key secondary outcome(s)
1. Serum indoxyl sulfate (IS) concentration in µmol/L measured using protein-precipitation LC–MS/MS using IS-d_4 as an isotope-labelled internal standard at baseline, month 6, and month 12. The outcome is the change in concentration from baseline.

2. Serum p-cresyl sulfate (pCS) concentration in µmol/L measured using protein-precipitation LC–MS/MS using pCS-d_7 as an isotope-labelled internal standard. at baseline, month 6, and month 12. The outcome is the change in concentration from baseline.

3. Serum trimethylamine N-oxide (TMAO) concentration in µmol/L measured using isotope-dilution LC–MS/MS using d_9-TMAO as the internal standard at baseline, month 6, and month 12. The outcome is the change in concentration from baseline.

4. Serum acetate concentration in µmol/L measured using LC–MS/MS separately following 3-nitrophenylhydrazine (3-NPH) derivatisation with an isotope-labelled acetate internal standard at baseline, month 6, and month 12. The outcome is the change in concentration from baseline.

5. Serum propionate concentration in µmol/L measured using LC–MS/MS separately following 3-NPH derivatisation using an isotope-labelled propionate internal standard at baseline, month 6, and month 12. The outcome is the change in concentration from baseline.

6. Serum butyrate concentration in µmol/L measured using LC–MS/MS separately following 3-NPH derivatisation using an isotope-labelled butyrate internal standard at baseline, month 6, and month 12. The outcome is the change in concentration from baseline.

7. Urinary albumin-to-creatinine ratio (UACR) in mg/g measured using urinary albumin (mg/l) divided by urinary creatinine (g/l). Urinary albumin is measured by immunoturbidimetry and urinary creatinine is measured by an enzymatic assay at baseline, month 6, and month 12. The outcome is the change from baseline; UACR is analysed on the log scale in the statistical analysis.

8. Sustained decline in eGFR of at least 30% from baseline measured using binary outcome (yes /no), defined as a reduction in eGFR of at least 30% from the baseline value and confirmed by a subsequent available eGFR measurement. eGFR is calculated from serum creatinine using the 2021 CKD-EPI creatinine equation. Measured at baseline and follow-up assessments at months 3, 6, 9, and 12; a decline of at least 30% must be confirmed by a subsequent available measurement during the 12-month follow-up.

Completion date
31/10/2026

Eligibility

Key inclusion criteria
1. Adults aged 18 years or older
2. CKD documented for at least 3 months
3.1. For CKD G1–G2, urinary albumin-to-creatinine ratio (UACR) of at least 30 mg/g on measurements separated by at least 3 months; or
3.2. For CKD G3a–G5, eGFR below 60 mL/min/1.73 m² persisting for at least 3 months
4. Clinically stable to permit outpatient follow-up
5. Able and willing to provide written informed consent
6. CKD G categories were G1 (eGFR ≥90), G2 (60–89), G3a (45–59), G3b (30–44), G4 (15–29), and G5 (<15) mL/min/1.73 m²
7. Albuminuria categories were A1 (<30), A2 (30–300), and A3 (>300) mg/g

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
85 Years

Sex
All

Total final enrolment
275

Key exclusion criteria
1. Current maintenance haemodialysis or peritoneal dialysis
2. Previous kidney transplantation

3. Acute kidney injury or acute systemic infection at screening
4. Active inflammatory bowel disease, major intestinal resection, or diagnosed gastrointestinal disease requiring ongoing immunosuppressive treatment
5. Systemic antibiotic exposure during the 8 weeks before baseline sampling
6. Initiation of probiotic or prebiotic supplementation during the 4 weeks before sampling
7. Current pregnancy
8. Inability to complete the scheduled assessments

Date of first enrolment
01/10/2024

Date of final enrolment
31/10/2025

Locations

Countries of recruitment
China

Study participating centre
Dezhou City Decheng District Traditional Chinese Medicine Hospital
Department of Nephropathy, Dezhou City Decheng District Traditional Chinese Medicine Hospital, Dezhou
Shandong
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Sponsor information

Organisation
Decheng District Traditional Chinese Medicine Hospital

Funder(s)

Funder type

Funder Name
Decheng District Traditional Chinese Medicine Hospital

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

IPD sharing plan summary

Published as a supplement to the results publication