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A study of genetic and environmental factors associated with kidney disease in people of African ancestry living in the UK

Submission date
04/05/2022

Recruitment status
No longer recruiting

Registration date
05/05/2022

Overall study status
Completed

Last Edited
16/04/2025

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
People of African or Afro-Caribbean ancestry are five times more likely to have kidney disease. They also develop kidney failure when they are about 10 years younger than white people. The connection between ethnicity and kidney disease is complex.
A gene pattern (APOL1-G1/G2 alleles) has been found which is common in people of African and Afro-Caribbean ancestry. We think this gene pattern prevents some forms of sleeping sickness which is why so many people of West African and Afro-Caribbean ancestry have these gene patterns. This gene pattern may make it more likely for some people to develop kidney disease (including particular types of disease: focal segmental glomerulosclerosis (FSGS), hypertensive-associated kidney disease). We do not completely understand why some people with these gene patterns develop kidney disease while others do not. We think there are additional factors including extra genetic changes and/or environmental triggers e.g. infection which lead to onset of kidney disease.
We would like to test your blood, urine and kidney tissue (if you have previously had a kidney biopsy) to get more information. This will allow us to develop tests to predict who is going to have kidney damage and find ways to prevent damage. You do not need to have a kidney biopsy if you have not already had one as part of your clinical care.

Who can participate?
For CKD Group:
You are of African or Afro-Caribbean ancestry and have kidney disease. This means that either your kidneys work less well than expected or that your kidneys leak protein or blood into your urine.
For Control Group:
You are of African or Afro-Caribbean ancestry and DO NOT have kidney disease

What does the study involve?
You will see one of the doctors or nurses who will answer any questions that you may have. If you agree to take part, we will ask you to sign a consent form and you will be given a copy to keep. We will then take extra blood, and urine from you. We will take a minimum of one extra

blood test from you and we will try to do these tests when you attend your normal appointments so you will not have any extra visits to the hospital or extra needles. We will take no more than 40 ml of blood from you at one point (4 tablespoons). There will be no repeat blood tests after this. We will also look at relevant medical records.
If you have had a kidney biopsy we will ask for your permission to retrieve any spare tissue that is available from storage for testing. You will not be asked to have any more kidney biopsy samples taken.

What are the possible benefits and risks of participating?
Your samples and information may help us to improve the treatment of people of African or Afro-Caribbean ancestry with kidney disease in the future.

There are no risks to you by taking part. The amount of extra blood that we take will not affect you. Occasionally people experience pain or bruising from having blood taken, but we will try to do this at the same time as your routine blood tests to minimise discomfort.

Where is the study run from?
The study will be running in the Renal Unit of King's College Hospital NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
March 2022 to November 2024

Who is funding the study?
The study is co-sponsored by King’s College Hospital NHS Foundation Trust and Kings College London and funded by AstraZeneca (UK).

Who is the main contact?
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Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
292365

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 292365, CPMS 52421

Study information

Scientific Title
APolipoprotein L1 in People of African ancestry Living in the UK: Exploration of genetic and environmental factors associated with Chronic Kidney Disease (APPLE-CKD)

Acronym
APPLE-CKD

Study objectives
Primary:
To establish if epigenetic DNA methylation patterns in the APOL1 gene promoter in renal tissue are comparable to peripheral blood mononuclear cells PBMC (or spleen) and urine in participants with CKD and controls (including deceased kidney donors) with APOL1 high and low-risk genotypes

Secondary:
1. To study the role of APOL1 genetics and epigenetics in the differentiation of inducible Pluripotent Stem Cells into kidney relevant cells
2. To develop a ‘clinical/genetic/epigenetic/inflammatory signature’ associated with CKD in people of African ancestry with validation

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/05/2022, North West - Greater Manchester West Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 2071048007; gmwest.rec@hra.nhs.uk), ref 22/NW/0100

Study design
Multicentre observational cohort

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Exploration of genetic and environmental factors associated with chronic kidney disease in patients of African ancestry

Interventions
In the study, plasma, serum, urine, pre-existing renal tissue and peripheral blood mononuclear cells (PBMC) will be collected from patients. These will be sent for further analyses for:
1. Genotyping and epigenetic analysis - for PBMC (spleen MCs), renal biopsy tissue, urine pellets cases and controls
2. APOL1 and inflammatory marker analysis - for plasma, serum, renal biopsy tissue, urine supernatant and urine pellets
3. Inducible Pluripotent Stem Cell (iPSC) analysis - for the cryopreserved PBMCs

Intervention Type
Genetic

Primary outcome measure
At a single time point:
1. APOL1 promoter DNA methylation patterns in renal tissue and PBMC (spleen) and urine (Cases only) measured using standard laboratory analysis
2. CKD disease phenotype measured using standard laboratory analysis

Secondary outcome measures
At a single time point:
Clinical characteristics from patient notes and laboratory records, inflammatory markers measured using novel proteomic methods

Overall study start date
01/03/2022

Completion date
30/11/2024

Eligibility

Key inclusion criteria
CKD cases:
1. Self-reported African ancestry

2. Aged ≥18 years
3. Willing and able to provide written informed consent
4. Chronic kidney disease (KDIGO Criteria)
5. Group 1: Without diabetic nephropathy or serological or biopsy-proven evidence of immune-mediated kidney disease
6. Group 2: With diabetic nephropathy or serological or biopsy-proven evidence of immune-mediated kidney disease

Controls:
1. Self-reported African ancestry
2. Aged ≥18 years
3. Willing and able to provide written informed consent
4. No CKD (estimated GFR >60 ml/min/1.73m² and urinary protein: creatinine <15mg /mol or albumin: creatinine ratio <3 mg/mmol or negative urine dip for protein).

Participant type(s)
Healthy volunteer, Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
240

Key exclusion criteria
For both CKD cases and controls:
1. Unable to provide informed consent
2. Pregnancy

Date of first enrolment
01/06/2022

Date of final enrolment
01/11/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

King's College Hospital NHS Foundation Trust
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Guys Hospital
Guys Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT

Sponsor information

Organisation
King's College Hospital NHS Foundation Trust

Sponsor details
Renal Unit
Denmark Hill
London
England
United Kingdom
SE5 9RJ
+44 20 3299 6625
rahman.ahmed1@nhs.net

Sponsor type
Hospital/treatment centre

Website
https://www.kch.nhs.uk/

ROR
https://ror.org/01n0k5m85

Organisation
King's College London

Sponsor details

Health Schools (Research Management & Administration Office),
Room 5.31, James Clerk Maxwell Building,
57 Waterloo Road
London
England
United Kingdom
SE1 8WA
+44 (0)207 8483224
reza.razavi@kcl.ac.uk

Sponsor type
University/education

Website
http://www.kcl.ac.uk/index.aspx

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The research team plans to disseminate the study research findings in the following settings:
• Conference presentation of study process and results at UK Kidney Week, American Society of Nephrology Conference or the European Renal Association conference and International Society

of Nephrology.
• Publication of results in a renal recognised high impact journal.

Intention to publish date
01/11/2025

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Cases version 1.1	25/04/2022	05/05/2022	No	Yes
Participant information sheet	Controls version 1.1	25/04/2022	05/05/2022	No	Yes
Protocol file	version 1.1	25/04/2022	05/05/2022	No	No
HRA research summary			20/09/2023	No	No