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IgA nephropathy study in Indians

Submission date	Recruitment status	[_] Prospectively registered
05/10/2017	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
11/10/2017	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
21/11/2023	Urological and Genital Diseases	

Plain English summary of protocol

Background and study aims
According to the World Health Organization (WHO) Global Status Report 2010, non-communicable disease (NCD) deaths are projected to increase by 15% globally and by 20% in South Asia between 2010 and 2020. Chronic kidney disease (CKD) is associated with an eight- to tenfold increase in cardiovascular (heart disease) mortality (death) and is a risk multiplier in patients with diabetes and hypertension (high blood pressure). A nationwide study conducted by the Indian Council of Medical Research found NCDs were responsible for 42% of all deaths. An Indian population-based study calculated the age-adjusted incidence of end stage kidney disease (ESKD) at 232 per million population. The Indian government has included care for kidney disease in its 12th 5-year plan cycle. IgA nephropathy (IgAN) is one of the leading causes of ESKD in India and worldwide. In IgA nephropathy (IgAN), Indians seem to develop disease early and of greater severity. There is an urgent need to understand the differences in disease progression and provide a prognosis to Indian patients with IgAN. The plan is to assess the differences in clinical presentation and outcomes, and apply newly developed methods for the assessment of kidney damage.

Who can participate?
Patients age 18 and over with primary IgA nephropathy

What does the study involve?
Patients are divided into low and high risk categories based on clinical and kidney tissue findings. These patients are followed up and based on the findings, they are divided into those who get worse faster (rapid progressors) and those who remain stable or worsen slowly (slow/non-progressors). Blood and kidney tissue samples are taken.

What are the possible benefits and risks of participating?
This study will help to understand the differences in the behaviour of this disease in an Indian population and allow better prediction of disease progression. The results will help with decision-making regarding the need for immunosuppression for aggressive IgA nephropathy. This study may also help define the role of targeted screening in at-risk communities, as whole-population based screening programs for kidney disease are not cost effective, especially in a developing country like India. There are no risks for participants as it is an observational study and only involves blood sampling.

Where is the study run from?
Christian Medical College (India)

When is the study starting and how long is it expected to run for?
May 2014 to December 2021

Who is funding the study?
1. Christian Medical College (India)
2. DBT India Alliance (India)

Who is the main contact?
Prof. Suceena Alexander

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
IA/CPHE/14/1/501501

Study information

Scientific Title
Why is IgA nephropathy aggressive in Indians? Study of the effect of galactose deficient IgA1, anti-glycan antibodies including immune complexes and complement components on the rate of progression of renal disease.

Acronym
GRACE- IgANI (Glomerular Research And Clinical Experiments- IgA Nephropathy study in Indians)

Study objectives
IgA nephropathy (IgAN) is the most common glomerular disease, and a frequent cause of end stage kidney disease. In India, IgAN is characterized by marked severity in a younger population.

IgAN in India occurs mostly in 20-30 year olds, which is in sharp contrast to the older age (35-40 years) of Caucasian and East Asian patients. Thirty to 40% of Indian patients have nephrotic syndrome and renal dysfunction at presentation, as compared to a slowly progressive disease with an actuarial survival of 80-85% over 10 yrs among Caucasians. A study showed a 10 year renal survival of 35% and a >20% decline of renal function over a mean follow up of 27 months in a cohort of IgAN patients. There is an urgent need to understand the differences in disease progression and provide a prognosis to Indian patients with IgAN. The plan is to characterize the differences in clinical presentation and outcomes, and apply newly developed methods for assessment of mechanisms of renal damage to patients. The trialists hypothesise that differential galactosylation and levels of serum Gd-IgA1 and/or AGlyIgA and activation of the lectin pathway of complement contribute to the progressive IgAN seen in Indians.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Pilot study: The Institutional Review Board (Silver, Research and Ethics Committee) of the Christian Medical College Vellore, 23/07/2014, Ref. No. IRB Min. No. 8962
2. Full study: The Institutional Review Board (Silver, Research and Ethics Committee) of the Christian Medical College Vellore, 24/06/2015, Ref. No. IRB Min. No. 9481

Study design
Observational prospective longitudinal cohort study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Chronic kidney disease and IgA nephropathy (IgAN)

Interventions
200 IgAN patients will be recruited and classified into low and high risk groups based on a validated risk score. High risk IgAN group are IgAN patients with an Absolute Renal Risk (ARR) score of ≥23 points. Low risk IgAN group are IgAN patients with an ARR score of <23 points. Equivalent number of healthy people and patients with other glomerulonephritis will serve as controls for standardisation methods in sera. Based on the rate of decline in estimated glomerular filtration rate (eGFR) during the average five-year follow-up, the primary clinical outcome in IgAN patients will be either rapid-progressors or slow/non-progressors. Antigen, antibody and complement staining in renal tissue at baseline will be correlated with clinical outcomes at follow-up. Molecular characterization of biomarkers in sera collected annually will be compared between the two groups. The trialists hope to incorporate these biomarkers into a risk score equation for better determination of disease prognosis in our population. They will also be bio-banking biological fluids for future biomarker analysis.

Intervention Type
Other

Primary outcome(s)

1. Levels of serum Gd-IgA1 and AGlyIgA including immune complexes, measured using ELISA at baseline and annually
2. Rate of progression of IgAN, measured by the rate of fall in estimated glomerular filtration rate (eGFR) estimated by the CKD-EPI creatinine equation measured annually till composite end-point or end of follow-up (average of five years)

Key secondary outcome(s))
1. Composite end-point of 50% decline in eGFR, ESKD or death, whichever occurs earlier, measured using CKD-EPI creatinine equation and ESKD defined as eGFR by CKD-EPI creatinine equation <15ml/min/1.73m2 and/or requiring renal replacement therapy
2. Co-deposition of components of the lectin and alternative pathway of complement activation in renal biopsies, measured by immunofluorescence and immunohistochemistry at baseline
3. Proteinuria, measured using 24 hour urine protein (g/day) at baseline and annually till composite end-point or end of follow-up (average of five years)

Completion date
31/12/2021

Eligibility

Key inclusion criteria
1. Age ≥18 years
2. Primary IgA nephropathy diagnosed by renal biopsy
3. Written informed consent
4. Willing to come for follow-up visits
5. Immunosuppression naive for three months prior to recruitment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
201

Key exclusion criteria
1. Secondary IgA nephropathy: e.g. due to lupus, liver cirrhosis, Henoch-Schonlein purpura
2. Glomerular filtration rate (GFR) as estimated by the CKD-EPI equation <10ml/min/1.73m2
3. Participants with systemic diseases that can affect the kidneys like diabetes, systemic lupus erythematosus, presence of HIV, HbsAg, HCV infections, malignancies etc

4. Participants with a history of psychological illness or condition which interferes with their ability to understand or comply with the requirements of the study

Date of first enrolment
09/03/2015

Date of final enrolment
31/12/2017

Locations

Countries of recruitment
India

Study participating centre
Christian Medical College
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632004

Sponsor information

Organisation
Christian Medical College

ROR
https://ror.org/00c7kvd80

Funder(s)

Funder type
University/education

Funder Name
Christian Medical College, Vellore

Alternative Name(s)
CMC Vellore, CMC

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
India

Funder Name
DBT India Alliance

Alternative Name(s)
The Wellcome Trust DBT India Alliance, DBT/WT India Alliance, DBT-Wellcome Trust India Alliance, Wellcome Trust/DBT India Alliance, Wellcome Trust DBt India Alliance, India Alliance, DBT/Wellcome Trust India Alliance, India Alliance dbt wellcome, WTDBT India Alliance

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
India

Results and Publications

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?
Results article	Baseline clinical, biochemical, and histopathologic characteristics	07/12/2020	21/11/2023	Yes	No
Results article	Three-year clinical outcomes	24/11/2021	21/11/2023	Yes	No
Protocol article		26/07/2018	21/11/2023	Yes	No