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Circulating biomarkers to detect sight-threatening diabetic retinopathy

Submission date	Recruitment status	[X] Prospectively registered
18/10/2018	Suspended	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
23/10/2018	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
28/06/2022	Eye Diseases	

Plain English summary of protocol

Background and study aims

At present, diabetic retinopathy, a serious complication of diabetes affecting the eye, is diagnosed and graded in severity by taking photographs of the retina at the back of the eye. In the UK people with diabetes are screened for diabetic retinopathy on an annual basis, costing about £50 per patient per year in England and Wales. While retinal screening is quite accurate in detecting diabetic retinopathy and discriminating between the sight threatening forms, this screening is cost prohibitive as a large-scale screening measure in low and medium income countries where the prevalence of diabetes may be as high as 20%. Other than diabetic retinopathy retinal screening there is currently no other rapid cost-effective means for providing routine screening of sight threatening diabetic retinopathy, which is the most common form of blindness in the working age. The most consistent risk factors for the development of diabetic retinopathy are long duration of diabetes, hyperglycaemia (high blood sugar) and hypertension (high blood pressure). However, there is substantial variation in the onset and severity of diabetic retinopathy that cannot be fully explained by hyperglycaemia and hypertension, suggesting that other risk factors have a role. The aim of this study is to measure existing biological molecules (biomarkers) found in the blood of people with diabetes that may identify people at risk of diabetic retinopathy with or without other diabetic complications. The development of a blood test would provide a rapid cost-effective, time-effective and patient friendly means of screening for sight threatening diabetic retinopathy at the population level, broadening access to care globally. Such a blood test would provide an initial screening tool that then could be confirmed with retinal imaging.

Who can participate?

Healthy volunteers and patients with diabetes aged over 40 with varying severity of diabetic retinopathy

What does the study involve?

The study involves a single visit to either of the centres where information is collected including height, weight, waist and hip and blood pressure measurements. All participants have about 20 ml of blood taken. The people with varying severity of diabetic retinopathy undergo retinal imaging and an OCT scan.

What are the possible benefits and risks of participating?
There are no immediate benefits but the results will help with the development of new diagnostics. During blood collection, the participants may experience mild pain of the needle pricking the skin and rarely bruising may occur.

Where is the study run from?
1. Moorfields Eye Hospital NHS Foundation Trust (UK)
2. Hillingdon Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
October 2017 to December 2021

Who is funding the study?
Global Challenges Research Fund and the UK Research Innovation (MRC)

Who is the main contact?
Prof. Sobha Sivaprasad
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Protocol serial number
SIVS1046

Study information

Scientific Title
Prospective multicentre discovery and validation of diagnostic circulating biomarkers to detect sight-threatening diabetic retinopathy

Acronym
Biomarker Study

Study objectives

The aim is to identify circulating biomarkers with the hope of developing a sensor that can be used to identify people at risk of sight threatening diabetic retinopathy with or without other diabetic complications by doing a simple blood test.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Oxford B Research Ethics Committee, 04/09/2018, ref: 18/SC/0477

Study design
Prospective multicentre case control study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Diabetic retinopathy

Interventions
Participant demographics and baseline characteristics will be captured as well as height, weight, waist and hip measurements and blood pressure. Retinal imaging and OCT scans will be performed on patients with varying degrees of diabetic retinopathy but not on healthy controls. Blood samples will be taken and measurements of HbA1c, total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL) , triglycerides (TG), serum creatinine will be determined by commercial biochemical automatic analyser. A panel of circulating biomarkers will be measured in the blood using commercially available ELISA kits.

Intervention Type
Other

Primary outcome(s)
Diagnostic accuracy of novel and existing circulating biomarkers for sight threatening retinopathy; the sensitivity, specificity and receiver operating characteristics (ROC) curves will be reported. As it is a cross-sectional study, there is a one-off blood collection, analysis and reporting.

Key secondary outcome(s))
1. Diagnostic accuracy of novel and existing circulating biomarkers for any diabetic retinopathy
2. Diagnostic accuracy of novel and existing circulating biomarkers for identifying people at risk of microvascular and/or macrovascular complications of diabetes
The sensitivity, specificity and receiver operating characteristics (ROC) curves will be reported. As it is a cross-sectional study, there is a one-off blood collection, analysis and reporting.

Completion date
30/12/2021

Eligibility

Key inclusion criteria
1. Adults > 40 years of age
2. Ability to give informed consent
3. Patient has to meet ONLY ONE of the criteria below to be included in this study:
3.1. Patient is not diabetic
3.2. Patient is Type 2 DM for > 5 years but no diabetic retinopathy in both eyes
3.3. Mild/Moderate/Severe NPDR with DMO defined as morphological OCT evidence of macular oedema in the worse eye in the last 12 months
3.4. Active PDR with or without diabetic macular oedema in the worse eye (newly diagnosed treatment naïve or being treated with PRP and/or VR surgery in the last 2 years)

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
538

Key exclusion criteria
1. Type 1 Diabetes Mellitus
2. Type 2 Diabetes Mellitus < 5 years with no diabetic retinopathy
3. Comorbidities such as liver disease, malignancy, acute infections, inflammatory processes, recent surgeries
4. Blood pressure systolic > 180 mmHg or diastolic > 110 mmHg
5. Pregnant and breast feeding women
6. Patient on corticosteroids or immunosuppression
7. Major ocular conditions like uveitis, glaucoma, AMD, vasculitis, occlusion etc in either eye
8. Any ocular conditions other than diabetic retinopathy/maculopathy affecting vision in either eye – for e.g. epiretinal membrane, vitreomacular traction etc
9. Cataract surgery or any ocular surgery in the last 3 months in either eye
10. Significant cataract affecting adequate fundus photographs in either eye
11. Mild/Moderate/Severe NPDR without DMO in worse eye (study eye)

Date of first enrolment
01/11/2018

Date of final enrolment
01/11/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Moorfields Eye Hospital NHS Foundation Trust
162 City Road
London
United Kingdom
EC1V 2PD

Study participating centre
Hillingdon Hospitals NHS Foundation Trust
Pield Heath Road
Uxbridge
London
United Kingdom
UB8 3NN

Sponsor information

Organisation
Moorfields Eye Hospital NHS Foundation Trust

ROR
https://ror.org/03zaddr67

Funder(s)

Funder type
Research council

Funder Name
Global Challenge Research Fund, Medical Research Council, UK

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Sobha Sivaprasad (sobha.sivaprasad@nhs.net). Type of data: fully anonymised processed dataset. The data will become available after the clinical study report is submitted to REC, for 5 years, by written request to Prof. Sobha Sivaprasad and approval obtained from Moorfields Eye Hospital, by encrypted data transfer for analysis on anonymised processed data. Consent from participants was obtained.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/06/2022	28/06/2022	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes