

Elucidating the high cardiovascular disease risk in South Asians: focus on monocyte phenotype and incretin hormones

Published: 02-03-2023

Last updated: 10-01-2025

Unravel the working of the immune system in South Asians, specifically the monocytes. We will also study whether the release of incretin hormones (GLP-1 and GIP) following a meal is lower in South Asians compared to Europeans. The latter we will...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON56245

Source

ToetsingOnline

Brief title

CAMI study

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym

cardiovascular diseases

Research involving

Human

Sponsors and support

Primary sponsor: Interne Geneeskunde

Source(s) of monetary or material Support: Beurs van Leids Universitair Fonds (LUF)

Intervention

Keyword: Glucocorticoids, Incretin hormones, Monocytes, South Asians

Outcome measures

Primary outcome

1. To compare immune cell composition between lean adolescent Dutch South Asian and BMI- and age-matched Dutch Europids
2. To compare the monocyte phenotype between lean adolescent Dutch South Asian and BMI and age-matched Dutch Europids
3. To compare functional and metabolic characteristics of monocytes between lean adolescent Dutch South Asian and BMI- and age-matched Dutch Europids

Secondary outcome

4. To compare glucocorticoid receptor sensitivity between lean adolescent Dutch South Asian and BMI- and age-matched Dutch Europids
5. To compare the release of incretins (GLP-1 and GIP) during a mixed meal tolerance test (MMTT) between lean adolescent Dutch South Asian and BMI- and age-matched Dutch Europids
6. To compare markers of glucose metabolism (glucose, insulin, C-peptide) during an MMTT between lean adolescent Dutch South Asian and BMI- and age-matched Dutch Europids
7. To compare markers of lipid metabolism (free fatty acids (FFA), triglycerides (TG), high-density-lipoprotein (HDL), total cholesterol) during

an MMTT between lean adolescent Dutch South Asian and BMI- and age-matched Dutch Europeans

Study description

Background summary

The worldwide increasing incidence of type 2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD) has significant health and economic implications. Interestingly, the vulnerability to develop CVD is higher in Dutch South Asians (from here on called: South Asians) than in Dutch Europeans. Several factors are suspected to contribute to this high CVD risk in South Asians, including higher prevalence of central obesity, insulin resistance and dyslipidemia as well as lifestyle factors such as lower amount of exercise and consumption of a diet high in ultra-processed foods. The higher susceptibility to develop central obesity and insulin resistance in the South Asian population would fit with increased sensitivity of the glucocorticoid receptor (GR) compared with Europeans, resulting in increased activity of the glucocorticoid system. Furthermore, dyslipidemia and inflammation are central risk factors for the development of atherosclerosis, the most important driver of CVD. Levels of C-reactive protein (CRP), a non-specific marker for low-grade inflammation in the body, were shown to be higher in South Asians compared to Dutch Europeans already just after birth. The fact that CRP levels are already higher in South Asian neonates suggests that genetic susceptibility may underlie the pro-inflammatory phenotype of South Asians. Up till now, only little is known about the regulation of the immune system of South Asians. Moreover, the phenotype of monocytes, the immune subset that plays a central role in atherosclerosis development, has also not been studied in South Asians so far. In addition, the underlying cause for the more proinflammatory phenotype is currently unknown in South Asians. Since this susceptibility further aggravates their high CVD risk, it is important to be further uncovered. Incretin hormones (glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP)), secreted by intestinal cells following a meal, have direct anti-inflammatory effects and the incretin system has not been studied in detail in South Asians compared to Europeans. Considering their high CVD risk, we hypothesize that Dutch South Asians have a relatively pro-inflammatory balanced immune system including more pro-inflammatory monocytes compared with Dutch Europeans and a lower release of anti-inflammatory incretin hormones following a meal, further contributing to their proinflammatory phenotype.

Study objective

Unravel the working of the immune system in South Asians, specifically the

monocytes. We will also study whether the release of incretin hormones (GLP-1 and GIP) following a meal is lower in South Asians compared to Europeans. The latter we will study with a mixed meal test followed by several blood withdrawals to study blood GLP-1 and GIP levels. In addition, we will study the sensitivity of the stress hormone receptor (glucocorticoid receptor) in both ethnicities by performing in vitro measurements in polymorphonuclear cells of both ethnicities.

We hope this study will give us more insight in the causes of the high cardiovascular disease risk in South Asians. Eventually, this may contribute to development of novel treatments to prevent cardiovascular diseases in this vulnerable population, targeting the immune system and/or incretin hormones.

Study design

This study is a cross-sectional study carried out at the Leiden University Medical Centre (LUMC). The study encompasses one screening phone call and half a study day that takes approximately 4.5 hours per participant. We will first study height, weight and body composition. Then, 3 questionnaires are taken. Then, blood is withdrawn for measurement of components of the immune system. Next, participants will consume a meal drink and blood is drawn at several time points afterwards to assess e.g. incretin hormones (GLP-1 and GIP) and hunger and satiety hormones (e.g. ghrelin, PYY), insulin, glucose and lipids in blood.

Study burden and risks

Participants will neither directly nor personally benefit from participating in this research project. At the same time, no large side effects are expected when taking part in this study. After informed consent, anthropometric measures will be taken, venous blood (130.5 mL) will be drawn for investigating the above-mentioned objectives and an MMTT will be performed to assess release of incretin hormones and insulin sensitivity. All measurements will be done in one study day that takes approximately 4.5 hours per participant.

Contacts

Public

Selecteer

Albinusdreef 2
Leiden 2333ZA
NL

Scientific

Selecteer

Albinusdreef 2
Leiden 2333ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Inclusion criteria

- Males and females of South Asian or Dutch European ethnicity
- Age from 18 to 30 years old
- BMI 18 - 25 kg/m²
- Capable of giving informed consent

Exclusion criteria

- (auto-) immune disease(s) including type 1 or 2 diabetes mellitus, chronic kidney disease, hepatic disease, inflammatory bowel disease, thyroid disease and rheumatoid arthritis.
- Genetic lipid-associated disorders such as familial hypercholesterolemia
- Any chronic renal or hepatic disease
- Use of medication known to influence glucose and/or lipid metabolism (e.g. beta-blockers, antidepressants, corticosteroids)
- Abuse of alcohol or other substances
- Smoking
- Vigorous exercise (>3 times/week)
- Milk or soy allergy
- Contraindications for the InBody720 scan, such as a pacemaker
- Participation in an intensive weight loss program or vigorous exercise program during the last year before the start of the study
- laboratory abnormalities that could point towards an underlying disease

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL	
Recruitment status:	Recruiting
Start date (anticipated):	26-06-2023
Enrollment:	48
Type:	Actual

Ethics review

Approved WMO	
Date:	02-03-2023
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO	
Date:	18-04-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO	
Date:	09-06-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO
Date: 26-06-2023
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
metc-ldd@lumc.nl

Approved WMO
Date: 04-09-2023
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
metc-ldd@lumc.nl

Approved WMO
Date: 18-04-2024
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
metc-ldd@lumc.nl

Approved WMO
Date: 31-12-2024
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL82859.058.22