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Evaluating the effect of hemodialysis modality on inflammation

Submission date
19/01/2025

Recruitment status
Recruiting

Registration date
21/01/2025

Overall study status
Ongoing

Last Edited
06/06/2025

Condition category
Nutritional, Metabolic, Endocrine

[_] 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
Patients suffering from chronic kidney disease (CKD) and diabetes mellitus (DM) are at an increased risk of developing cardiovascular complications and infections. Dysregulated NETosis may exacerbate pathogenic inflammatory pathways that are implicated in the complications of CKD, hemodialysis and diabetes. In light of the superior survival rates observed in patients treated with hemodiafiltration (HDF) compared to high flux hemodialysis (HFHD), alongside the documented dysregulation of NETosis in both hemodialysis and DM patients, this study aims to elucidate the effects of dialysis modality on NETosis activity in hemodialysis patients, stratified by diabetic status.

Who can participate?
Hemodialysis patients who are diabetic or non-diabetic undergoing HDF treatment. Healthy participants will be recruited as a control group.

What does the study involve?
The study involves changing the hemodialysis modality from HDF to HFHD for 3 weeks. NEtosis activation and markers will be measured before and after treatment and after conversion to hemodialysis treatment.

What are the possible benefits and risks of participating?
The institution's dialysis patients are routinely treated with HDF. Conversion to high-flux hemodialysis for 3 weeks is not expected to cause any complications. Many dialysis units in Israel and other parts of the world regularly treat patients with high-flux hemodialysis, demonstrating its safety and routine use. Therefore, changing the dialysis modality for this short period is not anticipated to pose any harm or risk to the patients. However, it is important to note that no specific clinical benefits are expected from this temporary change.

Where is the study run from?
Galilee Medical Center, Nahariya, Israel

When is the study starting and how long is it expected to run for?
November 2022 to December 2025

Who is funding the study?
This work was supported by the Russell Barrie Galilee Diabetes- SPHERE

Who is the main contact?
Dr. Kruzel-Davila Etty, Director of the Nephrology Department, Galilee Medical Center, Israel, ETTYK@gmc.gov.il

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
MOH_2022-09-22_0120059

Study information

Scientific Title
Evaluating the effect of hemodialysis modality on NETosis

Acronym
NETosis-neutrophil extracellular trap (NET)

Study objectives
Hemodiafiltration will reduce NETosis compared to high-flux hemodialysis

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 13/11/2022, Galilee Medical Center NHR (Route 89 Nahariya-Cabri, Naharyia, 22100, Israel; +972-4-9107267; Inbalp@gmc.gov.il), ref: 108-22 NHR

Study design
Non-randomized study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Hemodialysis patients

Interventions
Initially, the study was designed to evaluate NETosis activation and serum markers after 1 month of treatment with each modality (hemodiafiltration [HDF] and high-flux hemodialysis [HD]). However, due to the fact that patients in our unit are routinely treated with HDF, the intervention was adapted to reflect the clinical reality and to accommodate a shorter intervention period.

In the revised protocol, the study focused on measuring NETosis activation and serum markers as follows:
1. Hemodiafiltration (HDF) Phase: NETosis activation and serum markers were measured before and after a single HDF session, reflecting the baseline phase when patients were undergoing their standard HDF treatment.
2. High-Flux Hemodialysis (HD) Phase: After conversion to high-flux hemodialysis, NETosis activation and serum markers were assessed at 1 week and 3 weeks post-conversion. Measurements were conducted both before and after HD treatments during these time points.
The total intervention period was limited to 3 weeks, with the goal of capturing changes in NETosis activation within this timeframe. This adjustment ensures the study remains feasible while providing meaningful insights into the effects of HDF and HD on NETosis activation.

No clinical outcomes were measured. Neutrophils were isolated and stimulated with 100 nM PMA for 1 hour or left without stimulation. Neutrophils were stained for NETosis markers: Peptidylarginine deiminase 4 (PAD4), neutrophil elastase (NE), myeloperoxidase (MPO), Histone

H3 and dsDNA. Data were acquired using a flow cytometer. Serum levels of citrullinated histone H3 (citHIS), MPO and NE were measured using ELISA.

Added 06/06/2025:
Ten healthy participants will be recruited as a control group for both study arms. NETosis will be measured as described in the existing protocol. For each participant, two blood collection tubes will be used (6 mL each), totalling 12 ml per participant.

Intervention Type
Other

Primary outcome measure
NETosis activation and markers peptidylarginine deiminase 4 (PAD4), neutrophil elastase (NE), myeloperoxidase (MPO), histone H3 and dsDNA were measured using flow cytometry, and serum levels of citrullinated histone H3 (citHIS), MPO and NE were measured using ELISA, before and after treatment

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
14/11/2022

Completion date
31/12/2025

Eligibility

Key inclusion criteria
Hemodialysis patients

Added 06/06/2025:
10 healthy participants will be recruited as a control group for both study arms

Participant type(s)
Healthy volunteer, Patient

Age group
Mixed

Lower age limit
18 Years

Upper age limit
99 Years

Sex
Both

Target number of participants

20 incident hemodialysis patients: 10 diabetic and 10 non-diabetic patients

Key exclusion criteria
Patients with diseases that can affect NETosis such as autoimmunity, hemato-oncology, HIV and hepatitis C, B positive

Date of first enrolment
01/05/2023

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
Israel

Study participating centre
Galilee Medical Center
Route 89 Nahariya-Cabri
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Sponsor information

Organisation
SPHERE & Galilee Medical Center

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Sponsor type
Hospital/treatment centre

Website
https://www.gmc.org.il/

Funder(s)

Funder type
Research organisation

Funder Name
The Russell Berrie Galilee Diabetes SPHERE

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date
31/12/2025

Individual participant data (IPD) sharing plan
The datasets generated and/or analyzed during the current study will be available upon request from Dr. Etty Kruzel-Davila, ETTYK@gmc.gov.il

The type of data that will be shared:
• Baseline Clinical and Laboratory Characteristics:
Comprehensive baseline clinical and laboratory characteristics for both diabetic and non-diabetic patient groups, including demographic information, medical history, and relevant laboratory values.
• Raw Data of NETosis Assays:
Complete raw data from NETosis assays, including experimental measurements and results for all samples analyzed.
• NETosis Serum Markers:
Quantitative raw data for NETosis-associated serum markers, including citH3, MPO, NE, and other relevant markers, with separate datasets for diabetic and non-diabetic patients
• Timing for availability: The data will be made available at the time of manuscript publication.
• Whether consent from participants was required and obtained: Of course, all participants provided written informed consent prior to their inclusion in the study.
• Comments on data anonymization: To ensure medical confidentiality, patients' details were stored in a file coded by serial numbers, without any identifying information. This coded file will be used exclusively for statistical processing. A separate file containing the coding and identifying details of the patients will be accessible only to the principal investigator and will not be used for data processing or collection.
• Any ethical or legal restrictions: No ethical or legal restrictions.
• Any additional comments: No additional comments, aside from the request to edit the intervention part as specified above.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1		21/01/2025	No	No
Protocol file	version 2	06/06/2025	06/06/2025	No	No