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Effect of a ketogenic diet on the memory domain of cognition and its associated biomarkers in healthy individuals

Submission date
24/09/2025

Recruitment status
No longer recruiting

Registration date
28/09/2025

Overall study status
Completed

Last Edited
26/09/2025

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
The ketogenic diet is widely recognized worldwide as an effective weight loss regimen. While the effects of the ketogenic diet have been explored in relation to various diseases, its impact on the memory domain of cognition has not yet been thoroughly investigated. This study aims to explore the effects of the ketogenic diet on memory in healthy individuals. Furthermore, the study evaluated anthropometric measurements, body composition analysis, and blood ketone levels for both groups involved in the research.

Who can participate?
Healthy adult volunteers aged 25 to 45 years.

What does the study involve?
The study uses NIH Toolbox Cognition software to assess different aspects of memory, including working memory, episodic memory, and semantic memory, before and after a ketogenic diet intervention. Additionally, biomarkers were measured that are related to memory and synaptic plasticity, including serum cAMP, BDNF, and CREB levels. Also, epigenetic changes associated with the ketogenic diet were analyzed by quantifying microRNAs related to memory and synaptic plasticity at both baseline and after the intervention.

What are the possible benefits and risks of participating?
No benefits and risks given at registration

Where is the study run from?
Institute of Basic Medical Sciences, Khyber Medical University, Pakistan

When is the study starting and how long is it expected to run for?
October 2021 to December 2023

Who is funding the study?
Institute of Basic Medical Sciences, Khyber Medical University, Pakistan

Who is the main contact?
Principal investigator, Munaza Khattak, munazaakhan@hotmail.com

Contact information

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Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Office of Research, Innovation and Commercialization, Khyber Medical University DIR/ORIC/REF /25/00118

Study information

Scientific Title
Effect of ketogenic diet on memory domain of cognition and its association biomarkers in healthy individuals: quasi-experimental trial

Acronym
KETOMEMO

Study objectives
1. To assess cognitive function in the domain of attention and memory in individuals on a ketogenic versus a habitual diet
2. To investigate changes in serum brain-derived neurotrophic factor (BDNF) and cyclic AMP response element binding protein (CREB) levels in both the ketogenic diet and the control group
3. To find out and compare changes in serum expression of microRNA 132 and microRNA 124 in both the ketogenic diet and the control group
4. To explore the association of attention and memory performance of healthy individuals with their serum biomarkers.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 09/10/2021, Institute Review Ethics Board (IREB)- Institute of Basic Medical Science, Khyber Medical University Peshawar (Hayatabad, Peshawar, 25100, Pakistan; +92 (091) 9217703; irebibmskmu@gmail.com), ref: KMU/IBMS/IREB/9th meeting/2021/295

Study design
Non-randomized study

Primary study design
Interventional

Study type(s)
Quality of life, Efficacy

Health condition(s) or problem(s) studied
Cognition parameters in healthy individuals on a ketogenic diet

Interventions
For sample size calculation, the power calculation was based on the expected change in the memory function, which is the primary outcome. Sample size was calculated through the OpenEpi sample size calculator. Assuming a power of 80%, based on our primary outcome, i.e., expected change in the memory function, a confidence interval of 95%, and a ratio between the two groups of 1:1, a total of 66 participants (33 in each group) were required. Considering a 30% dropout rate, 86 participants needed to be enrolled in total (43 in each group: Ketogenic diet and control group). However, to cater for further dropouts due to the use of extended cognition software and possible issues in following the dietary intervention, the study enrolled 108 participants (54 in each group).

A 4-week quasi-experimental design was used with no follow-up due to financial constraints.

• After ASRB approval, ethical approval for the experimental procedure was obtained.
• Participants were recruited through brochures, flyers and word of mouth. Interested candidates were briefed and provided with the study information sheet. Those interested in the study were called for screening. Initial screening was done based on Age and BMI to determine eligibility, and at the start, they would be asked to check their step count on a pedometer. Those with a step count of less than 5000 steps/day will be recruited.
• Written informed consent was obtained from subjects (consent form can be provided if required)
• After recruitment, participants were randomized to two groups in a 1:1 ratio: the Ketogenic group (KD) and the Control group (CD). The ketogenic group was given a diet(≤5% carbs, 20-25% proteins and 70-75% fats) prepared by the researcher, whereas the control group (~50-60% carbs) were instructed to carry on their usual diet. It was a non-energy-restricted ad libitum diet. Intake of both groups was calculated by WinDiet software. Both groups were asked to refrain from any form of exercise and the use of supplements during the study period. Both groups completed all assessments at pre-intervention and post-intervention levels.
• In this study, recruitment was done after confirming they fulfilled the criteria of being healthy. (Healthy is defined in our study as an individual who has normal blood sugar, normal lipid profile, LFTs and no insulin resistance and has blood pressure within normal range and is not depressed).
• On day 0 (Screening day), 24-hour dietary recall, BP, pulse pressure, heart rate, and respiratory rate were recorded, a health screening questionnaire and Hamilton depression rating scale(HAM-D) were administered, and blood sampling was done for all the biochemical tests.
• Day 1 participants did anthropometric measurements, skin fold thickness measurement, bioelectric impedance analysis and cognition tests were performed on iPad-based software. Blood ketone bodies and FBS were measured.
• Participants would be given a ketogenic diet prepared by the researcher after recruitment, starting from Day 1 till Day 28.
• On Day 15, ketone bodies and BIA would be measured
• On day 29th post trial, all investigations were done again (Anthropometric measurements, BIA, Blood sample collection, cognition tests and ketone bodies were again measured).

Comprehensive cognition testing was performed for both groups using NIH Toolbox (NIH-TB) Cognition Battery (version 2) for working memory, episodic memory, semantic memory, processing speed, cognitive flexibility, attention and inhibitory control, fluid cognition composite score, crystalline cognition composite score and cognitive function composite scores(total or global cognition) on Day 1 and Day 29th of the trial.

Comprehensive anthropometrics, skinfold thickness analysis, body composition analysis and biochemical analysis were done. cAMP, BDNF and CREB serum protein levels were assessed using ELISA at baseline and post-intervention for both groups. Baseline and post-intervention miRNA levels were assessed using an RNA extraction kit followed by RT-PCR and real-time qPCR for both groups.

Expertise and Training
NIH Toolbox (NIH-TB) Cognition Battery (version 2) was used for cognition assessment. Hands-on training was provided by Dr Syed Hamid Habib, Dr Muhammad Irfan and Dr Mifah Sethi

Dr Syed Hamid Habib, MBBS, PhD (Glasgow, UK,) PGD(Glasgow, UK), Associate Professor, Institute of Basic Medical Sciences, Khyber Medical University.
Prof Dr Muhammad Irfan, MBBS, MCPS (Psych), FCPS (Psych), CHPE, MS (Mental Health Policy and Services), PhD (Summa cum Laude). Professor and Head, Department of Mental Health, Psychiatry and Behavioral Sciences, Peshawar Medical College, Riphah International University – Islamabad
Dr Mifrah Rauf Sethi, Associate Professor and Head of the Department of Psychology, Riphah International University, Islamabad, helped and trained in the depression scale and NIH toolbox training.
Workshop on nutritional aspects of the trial, use of the Herpenden calliper, and the use of Windiet software was provided by:
Dr Sadia Fatima, PhD Human Nutrition(Glasgow, UK), Post Doc (Uclan, U K) Department of Nutritional Biochemistry, Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, Pakistan
Dietitian: Hafsa Zafar. Department of Nutrition and Dietetics in Rehman Medical Institute (RMI), Nutrition and Rehabilitation Unit (NRU), Khyber Teaching Hospital, helped and gave a training workshop on nutritional aspects of the trial, use of Herpenden calliper, and the use of Windiet software.

Intervention Type
Supplement

Primary outcome(s)
Memory was measured using the NIH Toolbox cognition software at baseline and endpoint of the trial

Key secondary outcome(s))
1. Serum brain-derived neurotrophic factor (BDNF) and cAMP response element-binding protein (CREB) levels were measured using the ELISA kit at baseline and endpoint of the trial
2. Serum MicroRNA 124 and 132 by quantitative PCR at baseline and endpoint of the trial

Completion date
15/12/2023

Eligibility

Key inclusion criteria
1. Age 25-45
2. BMI 18-29.9 Kg/m2

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
25 years

Upper age limit
45 years

Sex
All

Total final enrolment
108

Key exclusion criteria
1. Diabetes
2. Heart diseases
3. Disorders of fatty acid metabolism
4. Hypertensives
5. Thyroid problems
6. Liver dysfunction
7. Neurodegenerative diseases
8. Obstructive sleep apnea
9. Pregnancy
10. Lactation
11. Keto food allergies

Date of first enrolment
12/10/2021

Date of final enrolment
23/11/2023

Locations

Countries of recruitment
Pakistan

Study participating centre
Institute of Basic Medical Sciences, Khyber Medical University
Phase 5, Hayatabad
Peshawar

Pakistan
25100

Sponsor information

Organisation
Khyber Medical University

ROR
https://ror.org/00nv6q035

Funder(s)

Funder type
University/education

Funder Name
Khyber Medical University

Alternative Name(s)
, , KMU

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Pakistan

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during or analysed during the current study will be shared upon approval from the principal investigator, Munaza Khattak, munazaakhan@hotmail.com. Coded and anonymized datasets in Excel or SPSS files will be shared by Munaza Khattak or Dr Hamid Habib after registration within 7 months. Phys_munazakhattak@prime.edu.pk /munazaakhan@hotmail.com Or Hamid.habib@kmu.edu.pk /dr.hamidhabib@gmail.com.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			26/09/2025	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes