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Visual acuity and eye parameters in relation to body size, shape and composition, considering maternal undernutrition during pregnancy

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With 5 tables

Abstract: The purpose of our study was to examine the eye parameters in relation to body size, proportions and composition in healthy or age-related macular degeneration affected adults, considering maternal diet during pregnancy. Statistically significant smaller corneal radius was found in maternal undernutrition groups comparing with maternal normal nutrition groups ($p < 0.05$), but there was no significant difference in retinal parameters or vision ($p > 0.05$). Statistically significant smaller distal width of humerus and Frame index in both genders, shorter humerus, radius, femur and tibia length in males, lower height, sitting height and shorter fourth finger length in females was found in age-related macular degeneration maternal undernutrition group compared to healthy retina normal nutrition group ($p < 0.05$). Our study revealed that participants with higher stature, longer limbs, more robust skeleton and higher accumulation of fat on trunk as well as with higher absolute active mass had statistically significant lower chance to suffer from age-related macular degeneration (OR < 1.0; $p < 0.05$). Subjects which suffered from maternal undernutrition had steeper central corneal radius, but no clear changes in the retinal thickness, which determines maintenance of good visual acuity. Developmental programming theory was supported by anthropometric peculiarities of individuals with age-related macular degeneration in the maternal undernutrition group – subjects had smaller distal width of humerus and Frame index, males had shorter humerus, radius, femur and tibia and women had shorter fourth fingers. Taller subjects with longer limbs, higher Frame index, more abundant fat accumulation on trunk, higher absolute active mass had lower chance to suffer from age-related macular degeneration.

Keywords: age; adult; age-related macular degeneration; anthropometry; growth programming; maternal undernutrition

List of abbreviations

AMD – age-related macular degeneration
BCVA – best corrected visual acuity
BMI – body mass index
CI – conicity index
95% CI – 95% confidence interval
CNV – choroidal neovascularization
D – body density
GA – geographic atrophy
GC-IPL – ganglion cell-inner plexiform layer
ILM-RPE – inner limiting membrane-retinal pigment epithelium
MNG – maternal normal nutrition group
MUG – maternal undernutrition group
N – number of subjects
IOP – intraocular pressure
OCT – optical coherence tomography
OCTA – optical coherence tomography angiography
OD – right eye, lot. *oculus dextra*
OS – left eye, lot. *oculus sinistra*
OR – odds ratio
RCOR – recalculated odds ratio
RNFL – retinal nerve fiber layer
RPE – retinal pigment epithelium
SD – standard deviation
WHR – waist-to-hip ratio

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1 Introduction

Maternal and child undernutrition remains a major global health concern (Black et al. 2013; Stephenson et al. 2018; Young & Ramakrishnan 2020; Victora et al. 2021). A significant part of the world was still experiencing famine in 2023, it has increased by 10% compared to 2022 (Global Food Crisis: What You Need to Know in 2023 – European Commission, n.d.). In developed countries, the issue of maternal undernutrition before and during pregnancy remains relevant, and various restrictive diets are becoming more popular as methods of weight loss (Yang et al. 2021; Yin et al. 2023; Yannakoulia & Scarmeas 2024).

Preconception and periconception periods are critical for fetal growth and health in both childhood and adult life (Roseboom et al. 2006; Black et al. 2013; Parlee & MacDougald 2014; Fleming et al. 2018; Öztürk & Türker 2021). Disturbances in periconceptional period program short-term and long-term consequences (Barker 2007; Black et al. 2013; Padmanabhanet al. 2016; Fleming et al. 2018; Koletzko et al. 2019; Moholdt & Hawley 2020; Öztürk & Türker 2021). Environmental factors such as heat, air pollution, maternal stress, chronic diseases, and nutrition are critically important for fetal growth and programming of health in later life (Roseboom et al. 2006; Black et al. 2013; Padmanabhan et al. 2016; Fleming et al. 2018; Stephenson et al. 2018; Öztürk & Türker 2021). Such developmental programming is non-genomic, but phenotypic advantage and allows match the organism's responses to the environmental conditions that are likely to prevail in later life; inappropriate growth programming, however, increases the subsequent risk for chronic disease (Bateson et al. 2014). It is known that exposures in early life play a key role in the development of various metabolic diseases for adults (Barker 2007; Padmanabhan et al. 2016; Mandy & Nyirenda 2018; Kinra et al. 2020; Moholdt & Hawley 2020; Li et al. 2022).

Maternal undernutrition, characterized by inadequate nutrient intake or imbalance during pregnancy, is a potent environmental stressor with profound implications for offspring health and well-being. Changes in fetal glucose and insulin homeostasis emerge under such circumstances to conserve energy for survival under conditions of insufficient nutrition. Severe starvation throughout in utero development leads to long-term adaptive alterations in glucose-insulin metabolism, including reduced insulin secretion and insulin resistance. These changes may enhance survival under conditions of nutritional deprivation during postnatal life because of the increased capacity to store fat (Wells 2011; Arage et al. 2022). The influence of malnutrition on offspring during the early developmental period has been substantiated by studies of naturally occurring periods of famine, such as the Dutch hunger of 1944–1945 (Lumey et al. 2007). There is evidence that even a relatively short period of fasting during pregnancy can cause metabolic rearrangements in growing fetuses (Ravelli et al. 1998).

As a result of evolution, mammalian embryos have responded to stressful environments by adjusting their organ and tissue development (Parlee & MacDougald 2014). Under conditions of deprivation in the early period of growth, the organism programs itself to save resources at the expense of non-vitally important organs. The brain, heart, and kidneys are protected against these deficits (Gluckman et al. 2016). Adequate nutrient intake before and during pregnancy is critical for neurodevelopment in the offspring (Cortés-Albornoz et al. 2021).

The retina transmits impulses to the brain and enables vision. Vision is one of the most important sensory functions in humans. The retinal layer changes with age. Age-related macular degeneration (AMD) is one of the leading causes of blindness all over the world in older adults and constitutes 8.7% of all types of blindness worldwide (Ruia & Kaufman 2024). Many studies have investigated the possible factors that increase or decrease the risk of AMD. Most studies have investigated the use of multivitamins in patients with different types of AMD (Evans & Lawrenson 2023). The third update of the review on the effects of supplements on AMD showed that antioxidants and minerals may reduce progression of AMD (Evans & Lawrenson 2023). Little is known about the impact of maternal undernutrition on changes in the aging retina of the offspring. Some studies have revealed that nutrition during the early growth period has an impact on changes in eye structure; however, they investigated only the anterior segment (Yamashita et al. 2019).

There is some data on the association of refraction errors and ocular biometry with personal weight, height, and body mass index (BMI) (Nangia et al. 2010; Xu et al. 2011; Wei et al. 2021). There is a lack of research explaining the linkage of anthropometric indices with retinal parameters and diseases, which is more valuable when analyzing growth programming theory.

In our experimental study with the offspring of rats from undernourished mothers, a change in outer retinal layer and Müller cells was observed (Laurinaviciute et al. 2022). Another study by our colleagues substantiated the influence of nutritional deficiency in the early development period on changes in the metabolism of adult rats and stated that maternal caloric restriction prior to pregnancy has an impact on body weight gain in adulthood (Araminaite et al. 2014). These findings inspired us to study humans as well and look for possible links between changes of the adult body and eye caused by nutritional deprivation during early development. However, the eyes are part of a crucial nervous system, so we hypothesize that the developing body prioritizes the allocation of its energy resources to ensure that the most essential functions are supported first, sacrificing less important body parts.

To our knowledge, no other study has examined the role of undernutrition in the preconception and periconception periods for adult vision and eye changes in relation to body composition characteristics in later life. Our research seeks

to advance our understanding of the growth programming theory and its implications for the eye health of older adults.

The aim of our study was to examine visual acuity and eye parameters (including retinal thickness) in relation to body size, proportion, and body composition in healthy or age-related macular degeneration (AMD) affected adults, considering the maternal diet during pregnancy.

Our research tasks were:

1) To compare visual acuity and parameters of the anterior segment and retina of the eye between healthy individuals and the AMD group, taking into account maternal diet during pregnancy; 2) to compare anthropometric parameters of body size, vertical and transverse dimensions, and body shape between healthy individuals and the AMD group, taking into account maternal diet during pregnancy; 3) to establish correlations between age, anthropometric parameters, and the thickness of the retinal layers measured by OCT in healthy retinas; and 4) to identify associations between age-related macular degeneration and patient age, sex, anthropometric indicators, and maternal nutritional status during pregnancy (regression analysis).

2 Methods

A total of 141 patients (49 men and 92 women) with a mean age of 71 years (SD = 8), ranging from 50 to 90 years, were included in the current study, 85 of whom had healthy retinas, and 56 were diagnosed with AMD.

All subjects underwent eye examination at the Consultation Center of the Republican Vilnius University Hospital (Vilnius, Lithuania). Informed consent was obtained from all participants. This study was approved by the Lithuanian Bioethics Committee (No. 2021/2-1313-789) and conducted according to the principles of the Helsinki Declaration.

Data on the participants' medical health, nutrition, physical activity, cardiovascular risk factors, and mothers' nutrition were collected from the original questionnaire, laboratory testing, and physical examinations.

Participants were born in a period of 1933–1973, most of them (74%) born during World War II, postwar period, and Lithuanian occupations (Nazi occupation (1941–1944), partisan war (1944–1953), Soviet occupation (1940–1941 and 1944–1990). Historical circumstances were complicated: certain groups of people were forced to hide, survive deportations, food was restricted during the Nazi occupation (food cards were introduced), and under the influence of the Soviet economy, people started living better only after 1953 (Anušauskas 2015). Such circumstances suggest that some mothers of study participants may have experienced nutritional insufficiency.

We asked several differently worded questions about the mother's fasting (lasting at least three months) before and during pregnancy to ensure the accuracy of the answers. It was asked "whether the mother had to starve two months ahead and during pregnancy?" The answers were: "no", "moderately", "severely". We also asked, "if the mother had enough food two months ahead and during pregnancy?" The answers were: "yes", "no". Our study subjects were assigned to the undernourished group if they indicated moderate or strong agreement with the statements in the questionnaire that their mothers experienced starvation and did not have enough food.

A total of 164 people participated in the survey and 141 were included in the final study. Data on the gestational age and birth weight were also obtained.

All subjects underwent full ophthalmological examination of both eyes (right eye, lot. *oculus dextra* (OD), left eye, lot. *oculus sinistra* (OS), including best-corrected visual acuity (BCVA), measurement of refraction and keratometry (autokerato-refractometer), intraocular pressure (IOP) (air-puff tonometry with The Ocular Response Analyzer (AMETEK Reichert Technologies, Depew, NY), correction of IOP for both corneal hysteresis and corneal resistance factor [rigidity]), pachymetry (Cirrus 5000, Carl Zeiss Meditec Inc, Dublin, CA, 2016), evaluation of iris color (Martin scale), slit-lamp biomicroscopy and ophthalmoscopy (Zeiss) and *optical coherence tomography* (OCT) (Cirrus 5000, Carl Zeiss Meditec Inc, Dublin, CA, 2016). OCT was used to evaluate the retina: retinal nerve fibre layer (RNFL) (Optic Disk Cube 200 × 200), and macula scans: ganglion cell-inner plexiform layer (GC-IPL) and inner limiting membrane-retinal pigment epithelium (ILM-RPE) thickness (Macular Cube 512 × 128)). OCT imaging signal quality of ≥ 6 was considered acceptable. We used a spectral domain device to perform optical coherence tomography angiography (OCTA) (AngioVue Software Version 2017.1.0.151, Triton, Fremont, CA, USA).

Scan placement, segmentation lines, and presence of any retinal pathology (drusen, atrophy of the retinal pigment epithelium (RPE) or retina, choroidal neovascularization (CNV), epiretinal fibrosis, pigment epithelial detachment, edema, vitreomacular traction, and/or macular hole) were evaluated manually.

Subjects diagnosed with AMD according to OCT and OCTA scans were divided into AMD categories: 1 – early (drusen); 2 – late: geographic atrophy (GA) or CNV.

Anthropometric characteristics, including height, weight, vertical (sitting height, length of the humerus, radius, hand, second and fourth fingers, femur, tibia, and foot) and transverse (biacromial and bicristal breadths, biepicondylar breadths of the humerus and femur, and distal width of the wrist) measurements, circumferences (head, neck, chest, upper arm, forearm, waist, hip, mid-thigh, medial-calf, wrist), and skinfolds (submental, mid-axillary, chest, abdominal, suprailiac, subscapular, triceps, biceps, forearm, mid-thigh, medial-calf), were obtained using standard methods

for individuals wearing light clothing without shoes (Preedy 2012; Olds & Norton 2013).

Other anthropometric indices were calculated (Preedy 2012; Olds & Norton 2013):

1. *Indicators of body size, shape, proportions:*

Body mass index (BMI) = weight (kg) / height^2 (m).
Acromiocristal index = bicristal breadth (cm) × 100 / biacromial breadth (cm).
Length of legs (cm) = height (cm) – sitting height (cm).
Skelic index = (height (cm) – sitting height (cm)) / sitting height (cm) × 100.
Intermembral index = (humerus length (cm) + radius length (cm)) × 100 / (femur length (cm) + tibia length (cm)).
Brachial index = radius length (cm) × 100 / humerus length (cm).
Crural index = tibia length (cm) × 100 / femur length (cm).
Grant index = height (cm) / wrist circumference (cm).
Frame index = (biepicondylar humerus breadth (mm) / height (cm)) × 100.
Ratio of radius length to height = radius length (cm) / height (cm).
Ratio of tibia length to height = tibia length (cm) / height (cm).
Waist-to-hip ratio (WHR) = waist circumference (cm) / hip circumference (cm)).
Conicity index (CI) = waist circumference (cm) / 0.109 √ (weight (kg) / height (cm)).

2. *Indicators of adipose tissue topography and body composition formulas:*

The ratio of sums of the skinfolds of the upper and lower body parts = (submental (mm) + mid-axillary (mm) + subscapular (mm) + chest I (mm) + chest II (mm) + biceps (mm) + triceps (mm) + forearm (mm)) / (abdominal (mm) + suprailiac (mm) + mid-thigh (mm) + medial calf (mm)).
Central and peripheral skinfold ratio = (submental (mm) + midaxillary (mm) + subscapular (mm) + chest I (mm) + chest II (mm) + abdominal (mm) + suprailiac (mm)) / (biceps (mm) + triceps (mm) + forearm (mm) + midthigh (mm) + medial calf (mm)).
Body density (D) (Durnin & Womersley 1974) age > 50,
male: D = 1.1715 – (0.0779 × log S)
female: D = 1.1339 – (0.0645 × log S)
S – sum of the skinfolds (mm) = biceps (mm) + triceps (mm) + suprailiac (mm) + subscapular (mm).
Relative fat (passive) mass (PM%), W.E. Siri (1961) = ((4.95 / D) – 4.50) × 100.
Absolute passive mass (PM) = weight (kg) × PM (%) / 100.
Relative active mass (AM%) = 100 (%) – PM (%),
Absolute active mass (AM) = weight (kg) – PM (kg).

All measurements were obtained by one of the authors (G.L., trained and tested for intraobserver error) using the same standardized anthropometric devices (Siber Hebner, Switzerland): anthropometer, sliding caliper, spreading caliper, Holtain skinfold caliper, anthropometric measuring tape, and electronic scales Gamma (SOEHNLE, Germany; step – 0.05 kg).

The exclusion criteria for the study were as follows: eyes with intraocular surgery other than routine phacoemulsification, ocular trauma, media opacities that can affect the quality of diagnostic imaging, high myopia (i.e., 5 diopters), high hyperopia (i.e., 5 diopters), high amounts of astigmatism (i.e., > 3 diopters), any history of diabetic retinopathy, glaucoma, IOP > 21 mmHg, macular or neuro-ophthalmic disease, retinal/choroidal pathology on any line of the macular cube (except AMD), difficulties in cooperation with the examination, and filling out the questionnaire. There were no differences in other chronic diseases among the individuals in all groups ($p > 0.05$).

2.1 Data analysis

Statistical analysis was performed using the IBM SPSS Statistics software (version 27.0; SPSS Inc., Chicago, IL, USA).

To calculate the minimum sample size, we used literature data on the highest prevalence of AMD in non-Hispanic White Europeans, which was 7.3% (Schultz et al. 2021). Analysis resulted in a minimum sample size of 129 with a margin of error of 4.5%. The minimum sample size was calculated as follows (Snedecor & Cochran 1989):

$$n = \frac{Z^2 \cdot p \cdot (1-p)}{E^2},$$

where:

- n is minimum required sample size.
- Z is critical value corresponding to the desired confidence level (e.g., 1.96 for 95% confidence, 2.58 for 99% confidence).
- p is the sample relative frequency.
- E is the precision of the population probability estimation (the maximum (absolute) error).

Kolmogorov-Smirnov and Shapiro-Wilk tests were used to check the normality assumption of the distribution of the variables in the investigated population. Quantitative variables were described as median, minimum, and maximum when their distributions did not satisfy the normality assumption, and as mean and standard deviation when the normality assumption was satisfied. The independent samples t-test or nonparametric Mann-Whitney U test was used to compare quantitative variables between the two groups (according to the normality assumption), nonparametric Kruskal-Wallis test was used to compare quantitative variables between more than two groups (according to the normality assumption or small sample size). Qualitative variables were described using frequencies and percentages. The chi-square test was used to determine differences in categorical vari-

ables between the groups. Correlations were calculated using Pearson's or Spearman's rank correlation coefficient. Statistical significance was set at $p < 0.05$. Binary logistic and stepwise multivariate regression analysis was performed to predict the associations of age, maternal undernutrition, and anthropometric parameters with AMD.

3 Results

3.1 General characteristics

First, we divided the subjects into two groups according to the retinal condition (subjects who had healthy retina and diagnosed with AMD) and then separated the groups according to the mother's nutritional deprivation before and during pregnancy: maternal undernutrition group (MUG) and maternal normal nutrition group (MNG) (see Table 1).

In the healthy retina group 33 (38.8%) of subjects were in the MUG, 52 (61.2%) of them in the MNG. There were no differences in age (years) (MUG: mean age is 69 years (SD = 8); MNG: median age is 69 years (min = 55; max = 90)), gender (MUG n male/female (%): 14/19 (42.4/57.6); MNG n male/female (%): 22/30 (42.23/57.27), and gestational age (weeks) (MUG: median = 39, (min = 36; max = 40), MNG: median = 38, (min = 36; max = 41)) between the groups ($p > 0.05$). The gestational weight (g) was significantly lower but suboptimal in the MUG (MUG: median = 3000, min = 2500; max = 4000; MNG: median = 3500, min = 2500; max = 5300; $p = 0.0007$).

In AMD group 24 (42.9%) of subjects were in the MUG, 32 (57.1%) of them in had MNG. There were no differences in age (years) (MUG: median = 73 (min = 60; max = 88); MNG: median = 73 (min = 50; max = 83)), gender (MUG n male/female (%): 7/17 (29.2/70.8); MNG n male/female (%): 6/26 (18.8/81.3); gestational age (weeks) (MUG: median = 39, (min = 36; max = 40); MNG: median = 38, (min = 36; max = 41)) between the groups ($p > 0.05$). The gestational weight (g) was significantly lower but suboptimal in the MUG (MUG: median = 3100, min = 2800; max = 3800; MNG: median = 3400, min = 2800; max = 4200; $p = 0.005$).

Current eating frequency, type of commonly consumed food, type of food preparation, eating place, and snacking did not differ significantly between the investigated subjects ($p > 0.05$), which reduced the impact of nutritional characteristics on the results. There were no differences between the individuals in all groups in terms of other chronic diseases or education ($p > 0.05$).

3.2 Visual acuity, parameters of the anterior segment and the retina of the eye

Healthy retina group. Median BCVA was 1.0 similarly in both nutritional groups ($p > 0.05$). Eye pressure, pachymetry results, and iris color did not differ between nutritional groups ($p > 0.05$). Our study showed a significantly smaller corneal radius in the MUG group ($p = 0.048$). No other structures in the anterior segment of the eye were significantly different between groups ($p > 0.05$). OCT parameters revealed that the RNFL, GC-IPL, and ILM-RPE thicknesses did not differ significantly between the MUG and MNG groups ($p > 0.05$). Only ILM-RPE thickness in the outer temporal quadrant was very close to being significantly thicker ($p = 0.05$) in the MUG group.

AMD group. Median BCVA, as expected, was significantly worse than that in healthy subjects and was in the range of 0.4–0.5 similarly in both nutritional groups ($p > 0.05$). Eye pressure, pachymetry results, and iris color did not differ between nutritional groups ($p > 0.05$). OCT showed that the neuroretinal rim area of the optic nerve was wider in the AMD nutritional deficiency group than in the normal nutrition group (MUG, median (min; max): 1.4 mm^2 (1.06; 1.78); MNG, median (min; max): 1.24 mm^2 (0.82; 1.89). The distribution of AMD categories between the MUG and MNG groups was not significantly different ($p = 0.123$). We observed no statistically significant difference in ILM-RPE and GL-IPL thickness in all quadrants compared to the MUG and MNG ($p > 0.05$).

Comparison between MNG and MUG showed statistically significant smaller corneal radius in the MUG (MNG mean is 7.73 mm (SD = 0.26) and MUG mean is 7.57 mm (SD = 0.26); $p = 0.007$).

Table 1. Grouping of the subjects included into the study. AMD: age-related macular degeneration, MNG: maternal normal nutrition group, MUG: maternal undernutrition group.

Group	Total subjects (n = 141)							
Retina group	Healthy retina (n = 85)				AMD (n = 56)			
Maternal nutrition group	MUG (n = 33)		MNG (n = 52)		MUG (n = 24)		MNG (n = 32)	
Gender group	Male (n = 14)	Female (n = 19)	Male (n = 22)	Female (n = 30)	Male (n = 7)	Female (n = 17)	Male (n = 6)	Female (n = 26)

3.3 Anthropometric parameters of body size, proportions and body shape

3.3.1 Comparison of vertical and transverse dimensions of skeleton between four groups

Healthy retina group. Height and other vertical and transverse dimensions were not significantly different between the MUG and MNG ($p > 0.05$); descriptive statistics are presented in Table 2.

AMD group (Table 3). Height was lower in MUG males and females compared than in those with MNG (only in females significantly, $p = 0.019$). Some differences in body proportions were detected between the groups: MUG males had shorter radius, femur, and smaller distal width of the humerus ($p < 0.05$); MUG females had shorter radius, hand, second and fourth fingers, and foot ($p < 0.05$).

3.3.2 Comparison of vertical and transverse dimensions between four groups

We found a statistically significant smaller distal width of the humerus and frame index in the AMD MUG than in the healthy retina MNG in both genders ($p < 0.05$). The humerus, radius, femur, and tibia lengths were significantly shorter in the AMD MUG males than in the healthy retina MNG males ($p < 0.05$). Height and sitting height were significantly lower and fourth finger length was shorter in the AMD MUG females than in the healthy retina MNG females ($p < 0.05$).

3.3.3 Comparison of indices of adipose tissue topography and body composition

Weight, BMI, waist circumference, WHR, and CI were not significantly different between the four groups (healthy

Table 2. Comparison of anthropometric indices between healthy retina MNG, healthy retina MUG, AMD MNG, AMD MUG (separating men and women). AMD: age-related macular degeneration, MNG: maternal normal nutrition group, MUG: maternal undernutrition group.

Anthropometric Index (cm)	Group	Male Median (min; max)	Male *p*-value	Female Median (min; max)	Female *p*-value
Height	Healthy retina MUG	178.0 (159.3; 191.0)	0.147	160.0 (149.6; 172.1)	**0.047 a**
	Healthy retina MNG	177.8 (160.7; 185.4)		162.2 (146.7; 172.1)	
	AMD MUG	168.7 (155.6; 182.0)		155.1 (145.8; 165.8)	
	AMD MNG	170.5 (164.0; 180.3)		161.4 (150.1; 176.4)	
Sitting height	Healthy retina MUG	88.0 (76.8; 95.2)	0.631	80.9 (62.1; 89.3)	**0.01 a,c**
	Healthy retina MNG	88.5 (74.0; 93.4)		82.0 (72.5; 89.8)	
	AMD MUG	82.2 (78.0; 92.4)		79.0 (71.6; 82.3)	
	AMD MNG	85.3 (81.0; 94.0)		79.2 (72.7; 87.5)	
Humerus length	Healthy retina MUG	40.25 (33.1; 43.8)	**0.008 a,e**	32.3 (27.5; 40.0)	0.069
	Healthy retina MNG	37.6 (34.5; 43.8)		33.4 (26.6; 37.5)	
	AMD MUG	32.2 (28.4; 38)		32.6 (27.4; 37.0)	
	AMD MNG	35.85 (27.5; 41.0)		35.5 (25.0; 39.0)	
Radius length	Healthy retina MUG	27.25 (23.1; 29.2)	**0.045 a**	23.4 (20.6; 27.3)	0.082
	Healthy retina MNG	27.0 (24.5; 29.5)		23.9 (20.8; 27.0)	
	AMD MUG	24.0 (23.2; 27.0)		22.8 (20.6; 25.4)	
	AMD MNG	27.2 (25.0; 28.9)		24.3 (22.1; 28.2)	

Table 2. continued.

Anthropometric Index (cm)	Group	Male Median (min; max)	Male *p*-value	Female Median (min; max)	Female *p*-value
Hand length	Healthy retina MUG	17.4 (16.2; 19.2)	0.589	15.6 (13.9; 17,7)	0.138
	Healthy retina MNG	17.6 (15.4; 19.5)		15.8 (13.8; 17.3)	
	AMD MUG	17.3 (15.1; 18.2)		15.0 (14.5; 18.2)	
	AMD MNG	17.6 (16.6; 18.1)		16.1 (14.8; 18.5)	
Second finger length	Healthy retina MUG	10.6 (9.1; 12.4)	0.053	9.2 (7.2; 10.6)	0.054
	Healthy retina MNG	10.4 (9.6; 11.4)		9.4 (7.8; 10.4)	
	AMD MUG	10.0 (8.9; 10.7)		8.9 (8.1; 9.9)	
	AMD MNG	10.3 (8.4; 10.7)		9.5 (7.9; 10.8)	
Fourth finger length	Healthy retina MUG	10.8 (9.4; 12.6)	0.292	9.2 (7.8; 11.3)	**0.005 a,d**
	Healthy retina MNG	10.6 (9.8; 12.4)		9.5 (8.2; 10.3)	
	AMD MUG	9.2 (8.4; 11.6)		8.8 (7.8; 10.4)	
	AMD MNG	10.8 (8.7; 11.2)		9.4 (8.2; 11.2)	
Femur length	Healthy retina MUG	51.8 (45.5; 62.0)	**0.001 a,e**	46.3 (39.3; 54.2)	0.631
	Healthy retina MNG	52.1 (41.9; 58.5)		47.2 (39.2; 54.8)	
	AMD MUG	38.7 (36.5; 47.8)		45.7 (34.8; 55.5)	
	AMD MNG	50.3 (44.0; 54.5)		47.5 (34.4; 57.6)	
Tibia length	Healthy retina MUG	42.1 (36.6; 46)	**0.016 a,e**	38.0 (31.5; 43.7)	0.324
	Healthy retina MNG	41.7 (34.3; 47.0)		39.1 (31.5; 45.0)	
	AMD MUG	36.6 (34.1; 43.0)		37.5 (35.5; 41.2)	
	AMD MNG	38.0 (36.3; 47.7)		39.2 (31.2; 43.4)	
Foot length	Healthy retina MUG	27.1 (24.0; 29.0)	0.663	24.4 (21.2; 26.2)	0.167
	Healthy retina MNG	27.0 (24.2; 31.2)		24.5 (22.0; 26.3)	
	AMD MUG	26.8 (26.0; 27.5)		23.6 (21.2; 26.8)	
	AMD MNG	27.0 (24.2; 28.0)		24.2 (22.3; 27.1)	

Table 2. continued.

Anthropometric Index (cm)	Group	Male Median (min; max)	Male *p*-value	Female Median (min; max)	Female *p*-value
Distal width of humerus	Healthy retina MUG	8.5 (7.4; 9.4)	**0.011 a,e**	7.6 (6.7; 9.7)	**0.007 a**
	Healthy retina MNG	8.4 (7.1; 9.2)		7.9 (6.0; 9.4)	
	AMD MUG	5.4 (5.4; 8.7)		7.0 (3.4; 8.8)	
	AMD MNG	8.5 (6.2; 9.2)		7.0 (4.6; 8.6)	
Frame index	Healthy retina MUG	46.7 (40.9; 54.8)	**0.029 a**	47.4 (41.9; 60.8)	**0.013 a**
	Healthy retina MNG	47.3 (40.7; 51.4)		49.2 (37.9; 60.0)	
	AMD MUG	34.7 (29.7; 51.6)		45.2 (22.2; 53.2)	
	AMD MNG	49.2 (35.2; 53.5)		44.4 (30.6; 53.9)	

a – statistically significant between groups of healthy retina MNG and AMD MUG $p < 0.05$
b – statistically significant between groups of healthy retina MUG and AMD MNG $p < 0.05$
c – statistically significant between groups of healthy retina MNG and AMD MNG $p < 0.05$
d – statistically significant between groups of AMD MUG and AMD MNG $p < 0.05$
e – statistically significant between groups of healthy retina MUG and AMD MUG $p < 0.0$

Table 3. Comparison of significant anthropometric indices in AMD group (between MUG and MNG (separating men and women)). AMD: age-related macular degeneration, MNG: maternal normal nutrition group, MUG: maternal undernutrition group.

Anthropometric Index (cm)	Group	Male Median (min; max)	*p*-value	Group	Female Median (min; max)	*p*-value
Height	MUG	168.7 (155.6; 182.0)	0.602	MUG	155.1 (145.8; 165.8)	**0.019**
	MNG	170.5 (164.0;180.3)		MNG	161.4 (150.1; 176.4)	
Sitting height	MUG	82.2 (78.0; 92.4)	0.345	MUG	79.0 (71.6; 82.3)	0.645
	MNG	85.3 (81.0; 94.0)		MNG	79.2 (72.7; 87.5)	
Humerus length	MUG	32.2 (28.4; 38.0)	0.350	MUG	32.6 (27.4; 37.0)	0.059
	MNG	35.85 (27.5; 41.0)		MNG	35.5 (25.0; 39.0)	
Radius length	MUG	24.0 (23.2; 27.0)	**0.031**	MUG	22.8 (20.6; 25.4)	**0.013**
	MNG	27.2 (25.0; 28.9)		MNG	24.3 (22.1; 28.2)	
Hand length	MUG	17.3 (15.1; 18.2)	0.650	MUG	15.0 (14.5; 18.2)	**0.020**
	MNG	17.6 (16.6; 18.1)		MNG	16.1 (7.9; 10.8)	
Second finger length	MUG	10.0 (8.9; 10.7)	0.419	MUG	8.9 (8.1; 9.9)	**0.009**
	MNG	10.3 (8.4;10.7)		MNG	9.5 (8.2; 11.2)	
Fourth finger length	MUG	9.2 (8.4; 11.6)	0.336	MUG	8.8 (7.8; 10.4)	**0.003**
	MNG	10.8 (8.7; 11.2)		MNG	9.4 (8.2; 11.2)	
Femur length	MUG	38.7 (36.5; 47.8)	**0.030**	MUG	45.7 (34.8; 55.5)	0.629
	MNG	50.3 (44.0; 54.5)		MNG	47.5 (34.4; 57.6)	
Tibia length	MUG	36.6 (34.1; 43.0)	0.216	MUG	37.5 (35.5; 41.2)	0.510
	MNG	38.0 (36.3; 47.7)		MNG	39.2 (31.2; 43.4)	
Foot length	MUG	27.0 (24.2; 28.0)	0.972	MUG	23.6 (21.2; 26.8)	**0.049**
	MNG	26.8 (26.0; 27.5)		MNG	24.2 (22.3; 27.1)	
Distal width of humerus	MUG	5.4 (5.4; 8.7)	**0.043**	MUG	7.0 (3.4; 8.8)	0.602
	MNG	8.5 (6.2; 9.2)		MNG	7.0 (4.6; 8.6)	
Frame index	MUG	34.7 (29.7; 51.6)	0.065	MUG	45.2 (22.2; 53.2)	0.765
	MNG	49.2 (35.2; 53.5)		MNG	44.4 (30.6; 53.9)	

retina MNG, healthy retina MUG, AMD MNG, AMD MUG; men and women groups were separated) ($p > 0.05$).

The ratio of the sum of the skinfolds of the upper and lower body parts and relative fat (passive) mass was significantly higher, while body density and relative active mass were significantly lower in healthy retina MNG females than in AMD MNG females (see Table 4). There was no difference in these anthropometric indices between the MUG and MNG groups in the healthy retina and AMD groups ($p > 0.05$).

The central and peripheral skinfold ratios and absolute passive or active masses were not significantly different between the healthy retina (MNG and MUG) and AMD (MNG and MUG) female and male groups ($p > 0.05$).

Other measured anthropometric parameters that were not discussed and not presented in the table were not significantly different ($p > 0.05$).

3.4 Correlations between age, anthropometric parameters and thickness of retinal layers measured by OCT in healthy retinas

The older the participant, the lower the minimum GC-IPL was found ((r) = −0.54; $p < 0.001$). We found a weak negative age association with almost all GC-IPL quadrants, except the inferior quadrant (superior temporal, r = −0.41; superior nasal, r = −0.42; superior, r = −0.47; inferior temporal, r = −0.4; inferior nasal, r = −0.55). Age was also negatively correlated with average RNFL (r = −0.41; $p < 0.001$) and ILM-RPE thickness in the outer superior (r = −0.37), outer nasal (r = −0.4) and inner superior (r = −0.32) quadrants.

BMI was not significantly associated with ocular parameters ($p > 0.05$). A weak negative correlation was observed between wrist diameter and average, minimum, and superior nasal GC-IPL thicknesses (r = −0.35; r = −0.31; r = −0.37; $p < 0.001$). Conicity was negatively correlated with the

Table 4. Comparison of adipose tissue topography and body composition anthropometric indices between the healthy retina MNG, healthy retina MUG, AMD MNG, AMD MUG (separating men and women). AMD: age-related macular degeneration, MNG: maternal normal nutrition group, MUG: maternal undernutrition group.

Anthropometric Index	Group	Male Median (min; max)	Male *p*-value	Female Median (min; max)	Female *p*-value
Ratio of sums of the skinfolds of upper and lower body part	Healthy retina MUG	1.50 (1.06; 2.73)	0.500	1.43 (1.03; 1.90)	**0.016 a**
	Healthy retina MNG	1.69 (1.07; 2.52)		1.41 (1.24; 2.36)	
	AMD MUG	1.60 (1.40; 2.30)		1.30 (1.00; 1.90)	
	AMD MNG	1.80 (1.40; 2.20)		1.20 (1.00; 1.90)	
Body density	Healthy retina MUG	1.04 (1.03; 1.05)	0.133	1.01 (0.995; 1.05)	**0.034 a**
	Healthy retina MNG	1.04 (1.02; 1.07)		1.00 (0.995; 1.05)	
	AMD MUG	1.03 (1.02; 1.04)		1.01 (0.998; 1.04)	
	AMD MNG	1,03 (1.02; 1.06)		1.02 (1.00; 1.03)	
Relative fat (passive) mass%	Healthy retina MUG	25.39 (22.33; 33.00)	0.112	38.60 (23.03; 47.65)	**0.031 a**
	Healthy retina MNG	26.54 (12.18; 34.95)		42.91 (23.63; 47.25)	
	AMD MUG	28.93 (24.96; 36.77)		38.82 (26.07; 46.08)	
	AMD MNG	28.92 (19.16; 34.67)		37.67 (30.64; 44.51)	
Relative active mass%	Healthy retina MUG	74.61 (67.00; 77.67)	0.113	61.40 (52.36; 76.97)	**0.033 a**
	Healthy retina MNG	73.46 (65.05; 87.82)		57.09 (52.75; 76.37)	
	AMD MUG	71.10 (63.20; 75.00)		61.20 (53.90; 73.90)	
	AMD MNG	71.05 (65.30; 80.90)		62.30 (55.50; 69.40)	

a – statistically significant difference between groups of healthy retina MNG and AMD MNG, $p < 0.05$, adjusted by Bonferroni corrections.

thickness of the superior nasal and inferior quadrants of the GC-IPL (r = −0.35; r = −0.37, $p < 0.01$) (higher conicity indicates greater fat deposition in the abdominal region). We also observed that Skelic index negatively correlated with average and inferior nasal GC-IPL thickness (r = −0.35; r = −0.34; $p < 0.001$) (the longer leg was, the thicker nasal GC-IPL). The brachial index correlated negatively with ILM-RPE thickness in the outer temporal quadrant (r = −0.32; $p < 0.001$) (the lower index indicates the presence of a relatively short forearm in relation to the arm length).

We also observed a medium negative correlation between the corneal radius and forearm circumference (r = −0.56; $p < 0.001$) and a weak negative correlation with submental skinfold (r = −0.45; $p < 0.001$).

Finally, our study agrees with the known tendency of a negative correlation between age and visual acuity (r = −0.36; $p < 0.001$).

3.5 Associations of age-related macular degeneration with patient age, sex, anthropometric indicators and maternal nutritional status during pregnancy (regression analysis)

Univariate binary regression analysis showed that older participants had a higher risk of developing AMD ($p < 0.001$; OR, 1.161). Gender and maternal undernutrition had no significant influence on the presence of AMD ($p > 0.05$). However, our study demonstrated that higher stature, longer limbs (longer humerus, radius, second and fourth fingers, foot, leg), more robust skeleton (higher frame index), and higher accumulation of fat on the trunk (thicker chest II skinfold, larger trunk-total or trunk and limbs, or central and peripheral skinfold ratio), as well as higher absolute active mass (OR < 1.0; $p < 0.05$), had a significantly lower chance of suffering from AMD (see Table 5).

Table 5. Variables for AMD prognosis (univariate binary logistic regression analysis). 95% CI – 95% confidence interval, RCOR – recalculated odds ratio (1/OR; then OR < 1, how many times is lower), OR – odds ratio.

Variable	OR	95% CI	*p*-value	RCOR	Healthy retina group median (min; max)	AMD group median (min; max)
Age (years)	1.161	1.100–1.225	< 0.001	-	69 (52;90)	average 72 (SD 6)
Absolute active mass	0.961	0.930–0.994	0.022	1.041	53.1 (35.0;83.4)	47.0 (35.3;75.4)
Height, cm	0.939	0.903–0.977	0.002	1.065	165.8 (146.7;191.0)	161.2 (145.8;182.0)
Length of the leg, cm	0.939	0.886–0.995	0.035	1.065	83.1 (68.4;105.5)	80.9 (72.0;94.3)
Foot length, cm	0.934	0.884–0.986	0.014	1.620	25.2 (21.2;31.2)	24.5 (21.2;28.0)
Chest skinfold II, mm	0.925	0.876–0.976	0.004	1.081	22.0 (7.0;38.0)	18.5 (5.0;34.0)
Humerus length, cm	0.900	0.823–0.985	0.022	1.100	35.2 (26.6;43.8)	34.2 (25.0;41.0)
Frame index	0.854	0.791–0.923	< 0.001	1.170	47.8 (37.9;60.8)	44.0 (22.2;53.9)
Radius length, cm	0.830	0.698–0.988	0.036	1.200	25.0 (20.6;29.5)	24.1 (20.6;28.9)
Fourth finger, cm	0.617	0.415–0.918	0.017	1.620	9.8 (7.8;12.6)	9.3 (7.8;11.6)
Second finger, cm	0.564	0.356–0.891	0.014	1.770	9.8 (7.2;12.4)	9.4 (7.9;10.8)
Central and peripheral skinfold ratio	0.411	0.210–0.804	0.009	2.433	1.8 (1.1;4.1)	1.5 (0.8;3.3)
Trunk and limbs skinfold ratio	0.399	0.198–0.803	0.010	2.506	1.7 (1.1;4.0)	1.4 (0.7;3.1)

In stepwise multivariate regression analysis, only age, fourth finger length, and Frame index were associated with AMD. Older subjects had 1.17 times higher chance of suffering from AMD (OR, 1.167; 95% CI 1.096–1.242; $p < 0.001$). Subjects with longer fourth fingers had a 1.82 times reduced chance to have AMD (OR, 0.549; 95% CI 0.325–0.927; $p = 0.025$). A higher Frame index was associated with a 1.14 times reduced risk of developing AMD (OR, 0.877; 95% CI 0.803–0.958; $p < 0.004$).

In addition, univariate binary regression analysis for AMD severity revealed that higher WHR 1000 times) reduced the chance of having GA or CNV as a more severe stage of AMD (OR 0.001; 95% CI 0–0.785; $p = 0.043$).

4 Discussion

4.1 General findings

This study investigated the effects of maternal undernutrition on the ocular structures of aging offspring with healthy or damaged AMD retinas, in relation to body size, proportions, and composition. To our knowledge, this study is the only to investigate the coherence between a wide range of anthropometric body parameters and the eye retina in terms of maternal undernutrition. Most researchers have evaluated only one or a few basic anthropometric parameters in association with the retina (Yamashita et al. 2013; Von Hanno et al. 2022); however, none of them have evaluated the effect of maternal malnutrition in the early growth period.

Our results support the hypothesis that body adaptation to undernutrition programmed in the intrauterine period of growth could protect and help maintain good eyesight without any drastic changes in the critical eye structures while changing body size, shape, and composition.

D. J. P. Barker and other well-known investigators in the field of growth programming showed an association between maternal undernutrition and metabolic syndrome or cardiovascular diseases (Painter et al. 2005; Barker 2007; Barker et al. 2009; Padmanabhan et al. 2016; Mandy & Nyirenda 2018; Kinra et al. 2020; Moholdt & Hawley 2020). Several studies have discussed maternal nutritional deprivation as a strong provoking factor for obesity, hyperglycemia, and changes in lipid profiles in adulthood (Painter et al. 2005; Victora et al. 2008; Parlee & MacDougald 2014; Lee 2015; Padmanabhan et al. 2016; Moholdt & Hawley 2020). Meanwhile, our study showed that the eyes, as part of the nervous system, are better protected against changes caused by maternal malnutrition, resulting in changes in the body structure. To the best of our knowledge, no other study has examined the effects of nutritional insufficiency on eye structure.

Our study found lower gestational weight in subjects with maternal undernutrition, supporting the idea that maternal nutrition was inadequate and limited fetal growth during early development. Many authors confirmed maternal undernutrition and a lot of other risk factors for foetal growth restriction and lower birth weight therefore (Painter et al. 2005; Roseboom et al. 2006; Gluckman et al. 2016; Reynolds et al. 2019; Moreno-Fernandez et al. 2020). Severe stressors activate adaptive mechanisms that result in reduced growth or early birth (Gluckman et al. 2016). Activation of the hypothalamic-pituitary-adrenal axis may be linked to low birth weight and subsequent metabolic disease (Reynolds et al. 2001; Mandy & Nyirenda 2018). However, there is also controversial data: Capra et al. showed that birth weights were similar between maternal dietary groups (control and 50% undernutrition groups) (Capra et al. 2022).

4.2 Visual acuity, anterior segment of the eye and retinal parameters

Our study found significant changes in body size and composition in the offspring of mothers who were undernourished during pregnancy, although the BCVA did not differ between the maternal nutrition groups.

In our study only the corneal radius of all ocular parameters in subjects was associated with maternal undernutrition. The corneal radius was smaller in the MUG group, indicating steeper corneal curvature. The cornea is often steeper than the average under myopic (near-sightedness) conditions. Our data showed a 7.57 (SD, 0.26) corneal radius in the MUG. Some authors have reported significant correlations between refractive error and central corneal radius of curvature. Alhussain SHA et al. shared statistics where central corneal radius of emmetropes was 7.86 ± 0.29 mm, low myopes (−0.5 D to −2.99 D) was 7.69 ± 0.20 (Alhussain et al. 2022). In a previous study, corneal radius was positively correlated with body height (Jonuscheit et al. 2017) and BMI (corneas were flatter with higher BMI) (Nangia et al. 2010). In addition, our study showed a positive correlation between the corneal radius, forearm circumference, and submental skinfold. No similar results were found.

The retinal findings of our study confirm the results of our previous experimental study on the retina. Maternal nutritional restriction in the early growth period has no clear influence on changes in the ganglion cell layer (Laurinaviciute et al. 2022).

4.3 Correlations of anthropometric parameters with age and retinal layer thickness and their association with age-related macular degeneration

The evolutionary theory postulates that energy is distributed in the body in such a way as to supply vital organs, such as the brain, heart, and kidneys (Gluckman et al. 2016). According to our findings, we claim that during the growth programming process, organisms allocate energy to their eyes as an extension of the brain at the expense of the height and length of the limbs. Consistent with previous studies, we found females with lower height and sitting height in the MUG of the AMD group (Victora et al. 2008;

Yamashita et al. 2019). In the face of nutritional deprivation, the adaptive process occurs by reducing the contribution of offspring to somatic growth of the offspring (Gluckman et al. 2016). While vital organs remain undamaged, limb height and length may decrease without any life-threatening consequences. This idea is also supported by other findings across the groups: subjects in AMD MUG had a significantly smaller distal width and Frame index in both genders, significantly shorter upper and lower limbs: humerus, radius, femur, tibia in males, and fourth finger in females of healthy retina MNG.

The inverse association between AMD and height is consistent with the results of previous studies. A population–based survey in Korea has demonstrated that taller body height lowers the prevalence of AMD (odds ratio [OR], 0.89; 95% confidence interval [CI], 0.81–0.99) (Hwang et al. 2020). Regression analysis in our study also showed that the longer the number of peripheral limbs, the lower the risk of developing AMD. The Frame index, an indicator of skeletal size, was also associated with AMD; the higher the score, the less likely the patient was to have AMD. These findings support the evolutionary theory that survival under deprivation begins with the skeleton and outermost limbs. Greater height and longer limbs suggest that the individual experienced a healthy intrauterine period with adequate nutrient supply, whereas shorter limbs may indicate intrauterine insufficiency. To the best of our knowledge, such data has not been studied previously.

Contrary to other researchers' waist circumferences, there was no statistically significant difference between the nutrition groups (Li et al. 2022). Our study findings, such as the significantly lower chance of suffering from AMD for those with higher trunk-total or trunk and limb skinfold ratios, support the theory of the organism's adaptation as a tendency to accumulate visceral adipose tissue as a depot under conditions of deprivation (Gluckman et al. 2016). Visceral adipose tissue is very labile (active), and hormones that release fatty acids are activated (Lebovitz & Banerji 2005). Central obesity may be related to deprivation experienced during the early period of growth and may lead to metabolic problems; however, it could function as a protective depot of the body (Lebovitz & Banerji 2005). Mammals can shift energy storage from muscle to adipose tissue under dietary changes (Parlee & MacDougald 2014). This idea is reflected in our study's further findings: the ratio of the sum of the skinfolds of the upper and lower body parts was found to be higher in the early stage of AMD. Furthermore, in our study, a higher WHR was associated with an even lower risk of advanced AMD (GA and CNV). Similar tendencies were observed in some studies where macular pigment optical density was positively associated with body fat percentage; however, WHR was not evaluated (Alsaqr et al. 2023). Our research revealed that a higher absolute active mass is associated with a lower risk of developing AMD. Accumulated metabolically active fat may protect against more severe diseases. What is seen in our research is that active adipose tissue storage is sometimes a positive skill in the body under certain conditions of deprivation.

However, among women (probably due to a larger sample size or because the fatty tissue accumulates differently in men's bodies), differences also emerged between the healthy and damaged retina groups in the absence of early malnutrition. Women with a healthy retina accumulated more adipose tissue, especially in the upper body (indicated by a higher ratio of folds, active body mass, and lower body density). Hence, they have this metabolic feature, and when and why it appears is debatable.

In contrast with previous studies, we did not find any meaningful BMI distinction between different nutrition groups in healthy and AMD subjects and no BMI association with ocular parameters (Li et al. 2022; Von Hanno et al. 2022). Von Hanno et al. reported BMI negative significant effect for RNFL, GC-IPL and even outer retinal layers (Von Hanno et al. 2022). Consistent with our findings, BMI was not associated with AMD (Hwang et al. 2020).

In our study, only age was negatively correlated with retinal thickness. In contrast, data from the study by Hanno et al. showed an association between retinal thickness and sex and being overweight (Von Hanno et al. 2022). Yamashita et al. stated retinal central temporal area thickness association with body height (Yamashita et al. 2013). In contrast, height did not correlate with retinal layer thickness in our study.

We investigated patients who were diagnosed with AMD. AMD is associated with deficiency of certain substances in adult life (Chew et al. 2014; Evans & Lawrenson 2023). To our knowledge, there is no known research evaluating food restriction in pre-pregnancy and pregnancy periods and its impact on the onset of AMD in the aging retina. Based on growth programming theory, we hypothesized that retinal resistance or proneness to AMD could be influenced by maternal nutritional status during the early developmental period.

Maternal undernutrition has been increasingly recognized as a risk factor for a variety of long-term health conditions, though there is still a need for more direct studies linking maternal undernutrition to AMD. Undernutrition may impact the development of AMD through a range of mechanisms, including early-life nutritional deficiencies, oxidative stress, inflammation, and vascular dysfunction, all of which can contribute to the disease's pathophysiology in later life (Chew et al. 2014; Evans & Lawrenson 2023).

However, we did not find any significant association between maternal undernutrition and a higher chance of developing AMD risk. It is important to note that almost all the differences in anthropometric parameters between the dietary groups in our study were found in the AMD group. Findings support the idea that maternal nutrition influences fetal programming and lack of nutrients turns on a mode of

saving body's resources. Energy is concentrated to develop the most important systems and organs (central nervous system, eyes) at the expense of less relevant body parts. The consequences of this fetal adaptation are low birth weight and shorter limbs in adulthood, also a thrifty phenotype characterized by fat accumulation, especially on the waist.

We suspected an association between AMD type and undernutrition; however, maternal nutritional deficiency did not lead to a higher chance of developing a more severe type of AMD. However, no study has compared these results with those of previous studies. The main study describing the influence of nutrition on AMD still remains the Age-Related Eye Disease Study (2001, see Chew et al. 2014), however, this study also evaluated only the effect of usage of vitamins for those who suffer from AMD. Individuals taking antioxidant vitamins are less likely to progress to late AMD (Evans & Lawrenson 2023).

Our study revealed the effect of age on retinal changes, and the results indicated that age is associated with an increased risk of AMD (Chakravarthy et al. 2020). Age was negatively correlated with the retinal layer thickness. The older subjects had thinner RNFL, GC-IPL, and ILM-RPE in some quadrants. Our findings are supported by Von Hanno et al., who showed that retinal thickness was associated with age in all macular regions (Von Hanno et al. 2017) and that ganglion cell layer had a strong negative correlation with age (Von Hanno et al. 2022). Hoffmann et al. also reported that aging was associated with RNFL (Hoffmann et al. 2018).

5 Limitations of the study

Most subjects had their parents still alive, whom they could ask about their mothers' diets. However, there could still be a memory recall bias; therefore, we only included cases of self-reported moderate and severe maternal fasting. A notable limitation of this study was the small sample size. A small sample size can reduce the statistical power of the study, making it difficult to detect significant effects or differences, and can increase the margin of error. Another significant limitation was the large age range of participants. Although a wide age range can provide insights into age-related differences, it may also introduce variability that obscures the effects being studied. Moreover, in the methodology section, we described in detail the historical period in which our subjects were born, and we want to emphasize that even the youngest subjects – 50 years old – were born in 1972, when there was Soviet occupation and access to various foods was severely limited for some population groups. Given these circumstances, it is likely that some of the mothers of the study participants may have experienced periods of nutritional insufficiency.

6 Conclusions

1) Participants who stated that their mothers faced undernutrition during the pre-pregnancy and pregnancy periods had lower birth weights. 2) All subjects who experienced maternal undernutrition had a steeper central corneal radius but no clear changes in the retina, which determines the maintenance of good best-corrected visual acuity (BCVA). 3) Developmental programming theory was supported by anthropometric peculiarities of individuals with age-related macular degeneration (AMD) in the maternal undernutrition group; all subjects had smaller distal width of the humerus and Frame index, males had shorter humerus, radius, femur, and tibia, and females had shorter fourth fingers. Taller subjects with longer limbs (humerus, radius, second and fourth fingers, and foot), higher Frame index, more abundant fat accumulation on the trunk, and higher absolute active mass had a lower chance of developing AMD. A higher waist-to-hip ratio (WHR) reduces the risk of developing severe AMD. 4) Maternal undernutrition was not associated with a high incidence of AMD or advanced AMD.

Declaration of interest statement: The authors report no conflicts of interest.

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