Correlation between diet, body mass index, and lipid profile in Kosovar women treated for primary infertility

Fatjona Gashi,[1,2] Muhamet Kadrija,[3,4] Zafer Gashi,[2,5] Mila Arapcheska,[1] Shkelzen Elezaj,[6-8] Fitore Gashi,[2,9] Fitim Gashi,[2] Gentian Elezaj,[7] Liridon Elezaj[8]

[1]Faculty of Biotechnical Sciences, University St. Kliment Ohridski, Bitola, North Macedonia; [2]Biolab Medical Laboratory, Pejë, Kosovo; [3]Department of Public Health and Infectious Diseases, Sapienza University, Rome, Italy; [4]University of Gjakova "Fehmi Agani", Gjakova, Kosovo; [5]UBT College, Prishtina, Kosovo; [6]Universum International College, Pristina, Kosovo; [7]Outpatient clinic "UROMED", Pejë, Kosovo; [8]Regional Hospital "Mother Teresa", Pejë, Kosovo; [9]Family Medicine Center "Mother Teresa", Klina, Kosovo

Correspondence: Muhamet Kadrija, Department of Public Health and Infectious Diseases, Sapienza University, Rome, Italy and University of Gjakova "Fehmi Agani", Gjakova, Kosovo.
E-mail: muhamet.kadrija@uni-gjk.org.

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ABSTRACT

The increasing prevalence of female fertility requires the identification of potentially modifiable factors and non-pharmacological treatments. There is strong evidence that healthy preconception dietary patterns of women of reproductive age have a beneficial effect on fertility. In accordance with the hypothesis, the aim of the study is to evaluate the influence of diet on overweight and obesity in infertile women as well as the correlation of serum lipid concentration by making a comparison between three observed groups with different body mass index (BMI). A total of 107 women who were treated for infertility were investigated. Diet and food pattern survey, BMI, and lipidogram determination from venous blood samples were carried out. The determination of lipidogram parameters was carried out by enzymatic colorimetric test with the COBAS INTEGRA 400 apparatus. From the total number of patients included in the study (107), infertile women with abnormal BMI accounted for 26.16%, while fertile women with normal BMI accounted for 73.83% ($p<0.001$). The total cholesterol value for groups with BMI>25 kg/m^2 was 6.78 mmol/L ($p=0.031$). High triglycerides with increased BMI were observed (2.27 mmol/L *versus* 2.68 mmol/L) ($p=0.028$). Low-density lipoprotein-cholesterol had higher concentrations in obese women (n=28), and high-density lipoprotein-cholesterol had lower concentrations in women with BMI>25 km^2 ($p<0.05$). Western dietary patterns of nutrition results in obesity and increased BMI values in infertile women. Increased BMI has a positive correlation with lipid profile in obese infertile women.

Introduction

Infertility as a disease affects a couple's social, psychological, economic, and sexual well-being and is a significant global health issue. Infertility is often defined as a couple's failure to conceive after 12-24 months of unprotected intercourse. Primary infertility occurs when a couple has never been successful in conceiving, whereas secondary infertility occurs after a previously confirmed pregnancy.[1] Infertility affects 10-15% of couples worldwide. In 35% and 45% of instances, respectively, the female and male variables are to blame, while the remaining couples either have a mix of factors or experience idiopathic infertility.[2] Primary infertility and secondary infertility are the two categories of infertility.[3]

The increasing prevalence of impaired female fertility makes the identification of potentially modifiable factors and non-pharmacological treatments that can positively affect fertility-related outcomes an urgent need. As various nutritional factors have been found to influence female reproductive health, great interest is growing in understanding the relationship between them and related research.[4,5] Admittedly, there is an inherent difficulty in studying the potential effect of diet and nutrition in infertility, which is anyway unique to any other pathology or condition as it is affected by the status of two rather than one individual due to the multifactorial and extremely complex nature of reproduction.[6] In today's world, food is not only a means to obtain nutrients but also contains non-nutritive chemical substances that may occur either as environmental contaminants or as synthetic byproducts of food processing and packaging.[7]

Nutrition and obesity impact on female infertility

Nutrition is a critical factor in human survival. Reproductive performance is definitely influenced by food and type of nutrition. DNA replication and protein synthesis require a source of energy obtained through food consumption. Therefore, it is important for women to maintain a healthy and balanced diet in the preimplantation and periconception periods.[8] The availability of energy substrates can regulate the developmental processes of oocytes within the antral follicles by suppressing or inducing meiosis.[9] The unbalanced intake of calories and proteins for the wrong consumption of food, responsible for under- or overweight, leads to changes in ovarian function with subsequent increases in infertility. Variations in body weight in terms of overweight and obesity are associated with changes in energy balance and are also suspected to cause ovulatory disorders. High body mass index (BMI) is associated with unfavorable pregnancy outcomes, such as diabetes, hypertension, and premature births; unbalanced diets with a predominance of carbohydrates, fatty acids, proteins, vitamins, and micronutrients obviously exert a negative influence on ovulation. Moreover, nutritional factors can affect not only oocyte maturation but also embryo quality and implantation efficiency.[10]

Nowadays, the burgeoning prevalence of obesity has emerged as a global health conundrum, casting a shadow over myriad facets of human well-being.[11] Defined primarily by an excessive accumulation of adipose tissue, obesity is no longer merely a reflection of lifestyle choices; it has metamorphosed into a multifaceted disorder with profound implications on physiological and metabolic functions.[12,13] The complex metabolism of hormones, cellular processes, and anatomical structures that underpin female fertility is susceptible to perturbations, and obesity, with its widespread systemic effects, has been identified as a significant disruptor.[14,15] The intersection of these two health challenges paints a complex picture. On one hand, obesity, with its associated metabolic and endocrine aberrations, can directly impinge on the reproductive health of women.[16] On the other hand, the psychosocial ramifications of infertility can exacerbate lifestyle patterns conducive to weight gain, creating a vicious cycle that is challenging to disrupt. Infertility can be a source of profound psychological distress, impacting relationships, mental health, and overall quality of life.[17,18] Obesity's influence on female infertility is a topic of significant concern in reproductive medicine.[19]

The altered levels of adipokines in obesity, particularly the decrease in adiponectin and increase in leptin, are implicated in the pathogenesis of infertility. These changes can affect ovarian function, disrupt the hormonal balance necessary for ovulation, and impair endometrial receptivity.[20] In women of reproductive age, obesity is associated with various reproductive challenges, including impaired ovulatory function, reduced implantation and pregnancy rates, and increased miscarriage rates. These issues become more pronounced with advancing age, particularly in women approaching the upper limits of their reproductive years. For instance, women aged 38 years and older with obesity experience suboptimal reproductive performance, impacting fertilization rates, embryo development, and pregnancy outcomes.[21,22]

Circulating lipids and female infertility risk

Lipids appear to play a role in fertility. However, the mechanisms explaining the association between serum lipids and reproductive outcomes are not yet fully understood. The follicle is the functional unit of the ovary that protects and nourishes the growing oocyte. Studies have shown that lipid metabolism affects follicle development, oocyte maturation, and ovarian hormone function.[23] Cholesterol metabolism is critical to female fertility, and all growing cells require large amounts of cholesterol for membrane synthesis. Indeed, lipoprotein cholesterol is a substrate for ovarian steroidogenesis that plays an important role in hormone levels and the maintenance of pregnancy in mammals.[24] The large amount of cholesterol that must be transported to the follicular cells and ultimately to the egg can have an effect on female mammalian reproduction, so its deficiency and excess are both harmful.[25]

Aims and purpose of this study

Following the hypothesis, the purpose of the study is to evaluate the influence of diet on overweight and obesity and the concentration of lipids in the serum in women of the Rafshi Region of Dugagjin in Kosovo and evaluate the fertility ability of women by making a comparison between the three observed groups with different BMI.

The specific objective of this study is to verify the hypothesis of the influence of diet and lifestyle on the fertility of ethnic Albanian women from a region of Kosovo, based on the results of the comparison between three observed groups with different BMI and the changes in the values of lipid levels [total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C); triglycerides (TG) and low-density lipoprotein-cholesterol (LDL-C)].

Materials and Methods

This study was carried out at the Biolab Zafi Polyclinic in Klina and at the Medical Laboratory, Biolab-Zafi-F, Pejë, Kosovo, as well as in three specialized gynecological clinics (one in Klina and two in the city of Peja in Kosovo). A total of 107 women who were being treated for infertility were investigated. The control group consisted of 79 women who became pregnant during the period from May 1, 2023, to July 30, 2024 (15 months), while the second group that did not get pregnant during the 15 months was composed of 28 women who were under treatment for primary infertility. Positive pregnancy in the first group (control group) was confirmed by human chorionic gonadotropin (HCG) analysis, as well as, after 5 weeks, with an ultrasound examination by a gynecologist specialist. All participants were informed about the purpose of the study, benefits, procedure, and confidentiality of the research study, and informed consent was obtained from all participants in the study.

Inclusion criteria

The study included 105 women who were being treated for infertility, as they met the World Health Organization (WHO) criteria for primary infertility (more than 12 months of regular, unprotected intercourse without pregnancy). The first criterion for the women to be included in the study was the absence of a first pregnancy and that the same women tried continuously for this period of time to get pregnant but without therapeutic stimulation of the ovaries, and the second criterion was that the male factor (husbands) had normal parameters of human ejaculate according to WHO (2021).[26]

Exclusion criteria

The first exclusion criterion from the study was women younger than 27 years. The second exclusion criterion was clinically proven infertility due to uterine abnormalities, tubal factors, severe endometriosis, and genetic and autoimmune diseases. The third criterion is women with general endocrine diseases (pituitary, kidney, thyroid) or diabetes mellitus type 1. The fourth exclusion criterion from the study was infertile women due to the male factors such as oligozoospermia, astnozoospermia, and teratozoospermia or their combination.

Observed outcome measures

BMI was calculated as weight kg/height squared (kg/m²). In order to investigate the impact of diet on obesity and the findings of lipid status analyses, all women were grouped into 3 categories according to BMI: i) I group normal BMI 18.5-24.9 kg/m^2 (79 patents) (control group); ii) II group overweight 25-29.9 kg/m^2 (19 patients); iii) III group obese ≥30 kg/m^2 (9 patients).[27]

To determine the diet consumed by the patients included in the study as the usual daily foods, we used the semi-quantitative questionnaire for the frequency and type of food, which we designed ourselves. The questionnaire asked patients for information on the following: number of meals per day, breakfast, ways of eating meals, vegetables at each meal, and portions of fruit per day. Also, in the questionnaire, there were questions to be completed for the assessment of lifestyle and physical activity between the two groups (normal and abnormal BMI), such as assessment of physical activity, participation in sports, fitness, and ways of spending time free. To determine lipid concentrations, blood (venous) samples were taken from 107 patients, and after centrifugation, the serum was used to determine serum lipid concentrations on the COBAS INTEGRA 400 plus machine, which is an analytical instrument introduced in 2019 by Roche Diagnostics (Basel, Switzerland). Determination of lipidogram parameters was carried out by the method of the enzymatic colorimetric test. Reagent kits: CHOL2 (Cholesterol Gen.2), TRIGL (Triglycerides), HDLC4 (HDL-Cholesterol Gen.4), LDLC3 (LDL-Cholesterol Gen.3). Reference values according to kits are CHOL2≤6.2 mmol/L, TRIGL≤2.0 mmol/L, HDLC4≤1.8 mmol/L, LDLC3≤4.0 mmol/L. Dyslipidemia was defined as the presence of one or more abnormal serum lipid concentrations. Having obese patients with a high lipid profile, we also determined the atherogenic index of plasma (AIP), a logarithmically transformed ratio of TG/HDL-C, considered a marker of plasma atherogenicity. AIP was calculated using the following formula: log10 (TG/HDL-C). It can be classified according to the values obtained: <0.11 for low risk, 0.11-0.24 for medium risk, and >0.24 for high CVD risk.[28,29]

Statistical analysis

Data analysis involved entering all collected data into a Microsoft Excel sheet and performing analysis using SPSS Version 21.0. Descriptive statistics were used to express the data in terms of frequency and percentage. All values are presented as mean ± standard deviation or standard mean. Inferential statistics were performed using logistic regression to examine relationships between variables. The $\chi 2$ (chi-square) test of independence was used for the analysis. Comparison between mean values of analyzed parameters was done through an independent *t*-test. A p-value less than 0.05 was considered statistically significant.

Results

Since the sample was quite homogeneous in terms of nationality (female patients were all of Albanian nationality), it was not possible to obtain comparative data with other nationalities. The results reported are for 107 female patients undergoing fertility treatment. The results for diet and nutrition, physical activity, BMI, and the values obtained from biochemical analyses of serum lipids are presented in tabular form. From this total number during the assembly of their medical treatment for infertility, a control group was created of 79 women who achieved pregnancy and a second group of 28 female patients who did not achieve pregnancy and who continued with primary infertility treatment.

Table 1 details the main characteristics of the participants in the study according to BMI values, education and smoking. The frequency of infertile women with abnormal BMI is 26.16%, while that of women with normal BMI values is 73.83% (p<0.05). Based on the abnormal BMI results, the results showed that 17.75% were overweight (BMI=18.5-24.9 kg/m^2) and 8.41% were obese (BMI≥30 kg/m^2) (p=0.05). Most of the participants in the study had a bachelor's or master's degree from both groups (70.8 *versus* 58.6%) (p=0.021). Results were slightly higher in the proportion of women with abnormal BMI who had primary or secondary education (29.1% *versus* 37.8%) (p=0.039). Women with a higher BMI declared that they did not smoke in a larger percentage of their group, 75% compared to 35.5% of the group of women with a normal BMI (p=0.006).

Answers to all questions are added from the Microsoft

Office Excel program. The responses of the groups were then analyzed statistically. The χ2 (chi-square) independence test was used for the analysis. Table 2 shows the results from the survey (questionnaire form) for the assessment of the diet and the most consumed types of food in meals that can affect BMI. Based on the number of meals per day, women with increased BMI values are more (4-5 meals per day and >5 meals per day), 77% *versus* 66% of women with normal BMI ($p<0.05$). The way of eating and the duration of eating, such as eating in a hurry on foot, outside the house, and eating at the table with the family, were the options to answer the survey. There were significant differences in all three sub-questions ($p<0.05$). The group of women with abnormal BMI represented a larger percentage who ate at the table with family (55%) *versus* the group with normal BMI (18%). 91% of women with a higher BMI had breakfast every day, or in most cases, with a slightly significant difference among women with normal BMI (89%) ($p<0.05$). The fourth question was: what do you prefer to eat for breakfast? White bread is consumed more often in both groups (48% *versus* 52%). Consumption of white bread together with cereals increases in the percentage of women with in-

Table 1. The main characteristics of the participants in the study according to body mass index values, education and smoking.

BMI (kg/m^2)	Number (%)	Percentage (%)
Normal BMI women	79	73.83
Abnormal BMI women	28	26.16
BMI group overweight	19	17.75
BMI group obese	9	8.41
Education of normal BMI women grupe (n=79)	Primary/secondary school n=23 (29.1)	Bachelor/master studies n=56 (70.8)
Education of abnormal BMI women grupe (n=28)	n=11 (37.8)	n=17 (58.6)
Smoking of normal BMI grupe (n=79)	No n=28 (35.5)	Yes n=51 (64.5)
Smoking of abnormal BMI grupe (n=28)	n= 21 (75.0)	n= 7 (25.0)

BMI, body mass index.

Table 2. Assessment of diet, the most consumed types of food in meals that can affect body mass index (BMI), classified into two groups, normal BMI and abnormal BMI.

1. Number of meals per day	3 meals per day	4-5 meals per day	>5 meals per day
Normal BMI women (n=79), %	34	58	8
Abnormal BMI women (n=28), %	23	63	14
2. Ways of eating meals	In a hurry on foot, outside the house	Working and eating at the same time	At the table with family
Normal BMI women (n=79), %	34	48	18
Abnormal BMI women (n=28), %	28	17	55
3. Eating breakfast	Yes, everyday	No	Most cases
Normal BMI women (n=79), %	48	11	41
Abnormal BMI women (n=28), %	52	9	39
4. What do you prefer to have for breakfast	White bread	Cereals	Fruits
Normal BMI women (n=79), %	45	32	23
Abnormal BMI women (n=28), %	56	26	18
5. How often do you like to eat bakery products	Everyday	2-3 times a week	0-1 times a week
Normal BMI women (n=79), %	23	40	37
Abnormal BMI women (n=28), %	48	44	8
6. How often do you consume sweet foods (biscuits, cakes)	Everyday	3-4 times a week	0-1 times a week
Normal BMI women (n=79), %	18	35	47
Abnormal BMI women (n=28), %	36	38	26
7. Do you prefer burgers and pizzas over proper meals?	1-2 times a week	3-4 times a week	0-1 times a week
Normal BMI women (n=79), %	11	48	41
Abnormal BMI women (n=28), %	31	62	7
8. Vegetables to every meal	Rarely	Sometimes	Often
Normal BMI women (n=79), %	20	31	49
Abnormal BMI women (n=28), %	16	38	46
9. Portions of fruit per day	1 Portions	2-3 Portions	More 3 Portions
Normal BMI women (n=79), %	36	44	20
Abnormal BMI women (n=28), %	49	38	13

BMI, body mass index.

creased BMI (82% *versus* 77%) ($p < 0.05$). The consumption of white bread every day or 2-3 times a week at every meal was frequent in both groups of women, but the group of women with abnormal BMI had a significantly higher percentage ($p < 0.05$). Women with abnormal BMI are 92% *versus* 63% of women with normal BMI. To investigate how often they use carbohydrate-containing foods, the question asked was: how often do you consume sweet foods (cookies, cakes)? Women with increased BMI consumed sweet foods daily, or 3-4 times per week, more than women with normal BMI (74% *versus* 59%, respectively) ($p<0.05$). The seventh question was: do you prefer burgers and pizzas over proper meals? There was a higher percentage of women with abnormal BMI consuming 3-4 times per week compared to the group of women with normal BMI (62% *versus* 48%) ($p<0.05$).

The eighth and ninth questions were about the consumption of vegetables in meals and how many portions of fruit they consume per day. The answers about the frequency of consumption of vegetables as often and sometimes did not show significant changes ($p>0.05$) (84% *versus* 80%). The consumption of portions of fruit 2-3 times a day and with more than three portions a day was in percentage higher in women with normal BMI (64% *versus* 51%) than in women with abnormal BMI ($p=0.019$).

In Table 3, the results of the assessment of physical activity between the two groups (normal BMI and abnormal BMI) are shown. There was a higher percentage of women with high BMI who were not active in terms of physical activity (60% *versus* 46% of respondents from the group with normal BMI) ($p=0.018$). In the second question (how often do you do sports or fitness?), women with normal BMI had a higher percentage (59%) compared to women with increased BMI (29%) ($p=0.009$). The last question was about how they spent their free time. High percentages of the two groups of women with increased BMI and normal BMI watch TV and rest and use the phone during their free time (86% *versus* 83%, respectively), without significant differences ($p>0.05$). There were comparative differences in percentages in spending free time with friends: 27% of women with normal BMI *versus* 14% of women with increased BMI ($p=0.021$).

Table 4 shows the comparison of age, BMI, blood blood lipoproteins and TG in fertile and infertile female patients.

The age of the two groups of patients (30.5 *versus* 29.2) had no significant significance ($p=0.058$). The differences in the results between the two groups were in the value of BMI, with higher values in the group of infertile women (28.3 kg/m^2 *versus* 22.7 kg/m^2) ($p=0.002$). From the lipid profile, infertile women had higher concentrations of TC ($p=0.038$), TG ($p=0.019$), and also higher concentrations of LDL-C ($p=0.026$), but lower concentrations of HDL-C compared to controls (0.97 *versus* 1.82) ($p=0.021$).

Table 5 reports the calculation of the AIP in women with normal BMI and abnormal BMI. AIP can be easily calculated from the standard lipid profile. Low-risk values were <0.11. Overweight and obese group patients (group II and group III) had higher risk values (0.311 *versus* 0.509) ($p=0.001$).

Table 6 shows the comparison of age, period of infertility, and lipid parameters with BMI groups in fertile and infertile women (107). The average value of age in the sample of fertile women (n=79) was 26.7 (±2.6) years. The mean value and reported age in the sample of infertile women

Table 3. Assessment of physical activity between two groups (normal and abnormal body mass index).

Assessment of physical activity, %	I'm very active	I'm averagely active	I'm not very active
Normal BMI women (n=79)	11	43	46
Abnormal BMI women (n=28)	4	36	60
Doing sports, fitness, %	2-3 times a week	3-4 times a month	I do not do sports
Normal BMI women (n=79)	28	31	41
Abnormal BMI women (n=28)	17	22	61
Ways to spend free time, %	Watching TV, reading	Hanging out with friends	Rest and on the phone
Normal BMI women (n=79)	47	27	26
Abnormal BMI women (n=28)	55	14	31

BMI, body mass index.

Table 4. Comparison of age, body mass index, blood lipoproteins and triglycerides in fertile and infertile female patients.

Group	Infertile female (n=28)			Fertile female (n=79)			p*
Parameters	Mean	SD	Range	Mean	SD	Range	
Age (years)	30.5	3.6	29-42	29.2	4.2	27-35	0.058
BMI (kg/m^2)	28.3	2.17	27.5-32	22.7	1.8	18.5-24.9	0.002
TC (mmol/L)	6.08	1.2	4.5 -7.12	4.78	1.13	3.96-5.38	0.038
TG (mmol/L)	2.57	1.19	2.1-3.63	1.98	1.14	0.7-2.13	0.019
LDL (mmol/L)	4.26	1.22	3.97-4.56	3.74	1.41	3.35-4.12	0.026
HDL (mmol/L)	0.97	0.44	0.60-1.34	1.82	0.69	0.87-2.11	0.021

SD, standard deviation; BMI, body mass index; TC, total cholesterol; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein; *$p<0.05$ infertile group compared to control fertile group. Values are shown as mean ± SD. The differences in body mass index mean between groups were assessed using a *t*-test.

group II (n=19) was 29.2 (±4.2) and in group III (n=9) it was 31.8 (±5.2), which was different between groups with significance p=0.041. The results show significant differences between the groups in terms of the duration of years of female infertility (p=0.032). From the results of Table 5, the prevalence of hyperlipidemia was observed in patients with elevated BMI (n=28) in both groups >24 (9 kg/m^2 and ≥30 kg/m^2) compared to the control group, with BMI in normal values. Cholesterol values in fertile women (control group) were within the reference values (4.78 mmol/L), while mean values of TC for groups with BMI above normal (>24.9 kg/m^2) were higher (5.38 mmol/L and 6.78 mmol/L) with a significant difference (p=0.031). The prevalence of hypertriglyceridemia was lower in the control group of women with BMI in the normal range of 1.78 mmol/L, but the prevalence was higher in the two groups with increased BMI (2.27 mmol/L *versus* 2.68 mmol/L) (p=0.028). LDL-C had higher concentrations in both groups with higher BMI values (n=28) (4.19 mmol/L and 4.32 mmol/L) compared to the concentration of LDL-C in women of the control group (fertile women) (3.74 mmol/L) (p= 0.036), while HDL-C had lower concentrations in women with higher BMI values (group II and III) (1.11 mmol/L and 0.83 mmol/L) compared to women in the control with normal BMI, where the results from Table 5 show that the concentration of HDL-C was 1.62 mmol/L (p=0.041).

Discussion

Nowadays, there are numerous publications of scientific articles that deal with the relationship between diet and fertility. The conclusions and recommendations of these articles are that various components of diet and lifestyle can contribute to reducing the risk of fertility problems in the reproductive age population and are of great help in effective treatment for women with infertility. Overweight and obesity have increased globally in women in recent years. Evidence shows that obesity is mainly caused by unfavorable dietary habits, lifestyle, *etc.*[30] Understanding the direct link between food intake and female fertility is essential, as diet is directly implicated in the development of other chronic metabolic conditions, such as obesity, that have an impact on reproductive health.[31]

In our study, the studied group of patients was only of Albanian ethnicity; however, there is also a study from 2019 by Lilaj on 182 infertile Albanian women and concluded that in the investigated sample of infertile patients, 35% had a normal BMI and 65% of women were overweight or obese (BMI≥25 kg/m^2). From our results in the investigated sample (Table 1), the percentage of overweight or obese women (BMI≥25 kg/m^2) was 26.16%. This lower percentage of women with abnormal BMI in our study can be explained by the smaller number (107) in our truck included in the study, but the comparison between the group with normal BMI (control group) and the group with abnormal BMI was a significant difference (p≤0.001) (p values are not shown in the table). There are studies that highlight the complex relationship between obesity and female infertility.[32] In a prospective cohort study of 3029 subfertile couples, a linear decrease in spontaneous pregnancy rates was observed with each increase in BMI above 29 kg/m^2, indicating a 4% decrease in pregnancy rates per kg/m^2 increase in BMI.[31] Van der Steeg *et al*. highlighted the impact of obesity on female fertility and fertility treatments, emphasizing that treatment of obesity should be the initial goal for obese infertile women before starting fertility treatments.[33]

Profound changes in dietary habits can occur at different stages of life, but they usually appear together with changes in the social environment, such as the beginning of primary, secondary, or university education.[34] Our results showed that completing a higher education significantly reduced the probability of being overweight (BMI>25) (Table 1). The results were apparently the high-

Table 5. Calculation of the Atherogenic Index in women with normal and abnormal body mass index.

Group	I group normal BMI 18.5-24.9 kg/m^2 (79 patients)	II group overweight 25-29.9 kg/m^2 (19 patients)	III group obese ≥30 kg/m^2 (9 patients)	p
API	-0.010	0.311	0.509	0.001

AIP, atherogenic index of plasma.

Table 6. Comparison of age, period of infertility and lipid parameters with body mass index groups in fertile and infertile women (107).

Group	I group normal BMI 18.5-24.9 kg/m^2 (79 patients)			II group overweight 25-29.9 kg/m^2 (19 patients)			III group obese ≥30 kg/m^2 (9 patients)			p
Parameters	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	
Age (years)	26.7	2.6	26-31	29.2	4.2	27-35	31.8	5.2	31- 38	0.041
Infertility (years)	1.7	0.6	1.6-2.3	2.4	0.8	2.1-3.2	2.6	0.7	2.5-3.2	0.032
TC (mmol/L)	4.78	1.13	3.96-5.38	5.38	1.23	4.41-6.15	6.78	1.16	4.58-8.10	0.031
TG (mmol/L)	1.78	1.14	0.7-2.13	2.27	1.18	1.88-2.75	2.68	1.22	2.29-4.11	0.028
LDL-C (mmol/L)	3.74	1.41	3.35-4.12	4.19	1.30	3.77-4.38	4.32	1.15	4.17-4.98	0.036
HDL-C (mmol/L)	1.62	0.69	0.87-2.11	1.11	0.57	0.61-1.47	0.83	0.32	0.58-1.22	0.041

SD, standard deviation; BMI, body mass index; TC, total cholesterol; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein;*p<0.05 infertile group compared to control fertile group. Values are shown as mean ± SD. The differences in body mass index mean between groups were assessed using a *t*-test.

est in the percentage of women with normal BMI who had higher education (bachelor/master) (70.8% *versus* 58.6% of women with primary and secondary education; p=0.021). This effect has been identified for a group of people who are more likely to come from a low-income background. In our results (Table 1), there was a negative correlation between smoking and BMI in women with a higher BMI (35.5% *versus* 75%) (p=0.006). This significant value favors our hypothesis that this percentage is higher than smokers with a normal BMI and that those who smoke eat less food. Ginawi *et al*. had a different conclusion: obesity was more prevalent in former smokers and less prevalent in current smokers.[35] As current studies show, dietary patterns can have a major impact on the development of fertility disorders.[36] Dietary patterns can be defined as the amount, proportion, variety and/or combination of different foods and beverages in the diet, as well as the daily/weekly frequency of consumption.[37]

The western pattern has been shown to negatively affect fertility, and an inverse correlation has been observed in the context of the Mediterranean dietary pattern.[38] In women of reproductive age, MD (Mediterranean dietary) appears to reduce the risk of weight gain and insulin resistance, which may increase the likelihood of pregnancy. This is due to the fact that insulin directly affects the function of the ovaries; therefore, insulin sensitivity and glucose metabolism may have a significant impact on ovulation and fertility in women.[39] In Table 2, the results from the questionnaire of the patient's answers for the assessment of the diet are reflected. The most consumed types of food in meals that can affect BMI, classified into two groups, normal BMI and abnormal BMI, was the western model as the one who most often sees Albanian women who were undergoing infertility treatment. This was proven by the food patterns they consume, which may be the result of an increasing migration to the western countries of the Kosovar Albanian population, which is also connected with the frequent visits from the West to the family and *vice versa*, influencing the diet and frequent feeding according to the western diet model. In most of the questions from the questionnaire, women with abnormal BMI had significantly different results from the group of control women with normal BMI, such as number of meals per day, ways of eating meals, eating breakfast, what they prefer to eat for breakfast, how much and how often they like to eat bread and bakery products, how often they consume sweet foods (cookies, cakes), whether they prefer burgers and pizzas over proper meals, eating vegetables at every meal and how many portions of fruit they eat per day (p<0.005).

Based on the number of meals per day, women with increased BMI values are more (4-5 meals per day and >5 meals per day) (77% *versus* 66% of women with normal BMI; p=0.017). Concerning diet and duration of eating, the group of women with abnormal BMI who ate at the table with family was 55% compared to the 18% of the group with normal BMI (p=0.032). Taking breakfast every day or most of the time showed a slight significant difference between the two groups (p=0.043). Consumption of white bread together with cereals increases the percentage of women with increased BMI (82% *versus* 77%) (p=0.029). Safdar (2018) concluded that the frequent use of bread and its products influences the cause of obesity. Most bread products do not contain good-quality proteins, the quality of which can be damaged by processing and extreme cooling. They contain starch and fat instead of healthy nutrients like protein, vitamins, and minerals. Daily consumption of white bread causes low intestinal motility and high deposition of cellulite and fat, which in turn causes severe obesity.[40] Our results showed that the consumption of bread and pastries, especially traditional foods such as pie (the so-called *flija*) are traditional foods that are consumed the most by the Albanian population in Kosovo. These foods contain high amounts of trans fats and refined flour, contributing to obesity and abnormally high BMI values. In Table 3, we used these data to compare the physical activity and BMI of women who had experienced infertility and fertile women. There was a higher percentage of women with high BMI who were not active in terms of physical activity (60% *versus* 46% of respondents from the normal BMI group; p=0.018). The research by Saremi *et al.* revealed a significant correlation between physical inactivity and BMI in women with infertility. Notably, this study highlighted that physical inactivity, sedentary habits, and a high BMI each represent independent risk factors for infertility.[41] Table 3 shows the highest percentages of BMI in the group of infertile women who did not engage in any sports or fitness, while infertile women with abnormal BMI in a larger percentage (55% *versus* 47%) spent their free time watching TV or reading, which goes in favor of physical inactivity and contributes to obesity and an increase in BMI. The results shown in Table 4 are the biochemical analyses of lipoproteins and TG analyzed in the serum of 107 patients, divided into two groups of women with normal BMI and those with abnormal BMI. We should emphasize that the interpretation of our findings may be limited by the lack of published studies comparing lipid-related characteristics and female infertility when the cause of infertility is, in women with abnormal BMI, and according to our hypothesis, the increase in BMI of infertile women, which has contributed to the dietary pattern of obesity, excluding the genetic etiology of the increased BMI values of the group of infertile women (n=28) included in our study.

Our results (Table 4) showed higher concentrations of TC (4.5-7.12 mmol/L), TG (2.1-3.63 mmol/L) and LDL-C (3.97-4.56 mmol/L) in the group of infertile women (n=28), with abnormal BMI compared to the control group [fertile women, n=79; TC=3.96-5.38 mmol/L (p=0.038); TG=0.7-2.13 mmol/L (p=0.019); LDL-C=3.35-4.12 mmol/L (p=0.026)]. However, we had a negative relationship between BMI with abnormal values and HDL-C. HDL-C concentrations were lower in group I of women with abnormal BMI (0.60-1.34 mmol/L *versus* 0.87-2.11 mmol/L in women with normal BMI; p=0.021). Our results are in unison with those of other authors who examined the effects of BMI and lipid metabolism on embryo quality and pregnancy outcomes.[42] According to the findings, there was a direct relationship between BMI and the concentration of TC, TG, and LDL and a negative relationship between BMI and HDL.

In agreement with our findings, Tehrani *et al*.'s study documented a positive relationship between lipid profiles and low ovarian reserve.[43] Once again, we can speculate that the results of our research provide reliable mechanisms for the associations between lipid concentrations in infertile women with abnormal BMI and prolonging the period of primary infertility in obese women. The results of our study (Table 5) showed that women with pathological BMI had a significant increase in the AIP with increasing BMI (0.311 and 0.509) compared to fertile women with normal BMI (p=0.001). The authors conclude that the increased AIP values are a consequence of the increase in fat mass and the concomitant decrease in insulin sensitivity, associated with obesity, and have multiple effects on lipid metabolism.[44] Table 6 shows the different concentrations of lipoproteins in women with normal BMI and with abnormal BMI. There is a positive correlation between high concentrations of lipoproteins in infertile women based on abnormal BMI values (II group overweight 25-29.9 kg/m^2 and III obese group ≥30 kg/m^2. These findings correspond with previous research that has explained that abnormal circulating lipid metabolism affects the hormonal milieu, steroid synthesis, and ovarian and uterine function and has an impact on female reproductive function.[45] Another population-based prospective cohort study suggested that lipid concentrations in serum can be associated with a reduction in female fertility and a prolonged time until pregnancy.[46] This conclusion was also confirmed in our research, where women who had a longer period of infertility (2.1-3.2 and 2.5-3.2) were those with abnormal BMI compared to women with normal BMI (1.6-2.3) (p=0.032). Results of TC were higher in group III obese ≥30 kg/m^2 (n=9); TC=4.58-8.10. mmol/L compared to the results of 4.58-8.10 mmol/L in the II overweight group 25-29.9 kg/m^2 and the I group with normal BMI values 18.5-24.9 kg/m^2 where the values were 3.96-5.38 mmol/L (p=0.031). Some other studies prove that increased cholesterol concentrations have a negative effect on fertility. If a woman is exposed to a high-fat environment for a long time, lipid levels in the body's oocytes may increase and oocyte toxicity may occur, which may severely interfere with the process of oocyte meiosis and ultimately affect pregnancy.[21] Liu *et al.* found that oocyte cholesterol homeostasis in women may also be related to the developmental potential of the egg.[47]

In our research, the results of TG and LDL-C in infertile patients with abnormal BMI were of greater concentration [TG=1.88-2.75 *versus* 2.29-4.11 mmol/L, with statistically significant values between the groups (p=0.028), and LDL-C=3.77-4.38 *versus* 4.17-4.98 mmol/L (p=0.036)] (Table 6). Even Zhu *et al.* presented results similar to ours with an increase in the concentration values of LDL-C (mmol/L), TC (mmol/L), and TG (mmol/L) in serum; thus, the risk of infertility in women increased by 13%, 16%, and 16% respectively. However, these authors concluded that there was no indication that HDL-C (odds ratio: 1.00; 95% confidence interval: 0.887-1.128, p=0.999) was significantly associated with the risk of female infertility.[48] Our results showed that concentrations of HD-C (good cholesterol) were negatively related to high BMI values. The concentrations of HDL-C in the two groups of infertile women with abnormal BMI were lower (0.61-1.47 and 0.58-1.22 mmol/L) compared to the values of HDL-C in the group of fertile women (control group) (p=0.041). Low values pose a risk for cardiovascular disease as the concentration of HDL-C has several important functions, such as the transport of cholesterol from peripheral tissues to the liver, anti-inflammatory effects, apoptotic effects, mitigating the oxidation of lipo-LDL-C, and providing better antioxidant status.[49]

Conclusions

The western dietary model of nutrition results in obesity and abnormal BMI values. BMI with increased values has a positive correlation with lead concentrations in infertile women with obesity. A lack of physical activity, combined with a diet high in flour and carbohydrates, increases the concentration of lipids in women with an abnormal BMI. To conclude, we believe that these findings may lead to improvements in fertility assessment with the addition of lipid screening and some guidelines, such as increased medical check-ups and lifestyle changes.

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