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# Overweight and Obesity as the Risk Factors for Leukemia in the Mediterranean Countries

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## Abstract

It is known, that in countries with high and medium incomes, the proportion of people with overweight and obesity started to increase in the second half of the 20th century, as well as the incidence rate of Non-infectious Chronic Diseases (NCD). The study of risk factors for leukemia in the Mediterranean countries showed, that the incidence of leukemia for men was 2 times higher in countries with a higher Quality of Life (QOL); a higher percentage of men with overweight, obesity and hypercholesterolemia; a higher level of macronutrients, as on the whole as well as macronutrients of Animal Products (AP); a higher level of consumption of AP and Alcoholic Beverages (AB). Energy and proteins of animal products, beef and iron of animal origin, as well as hypercholesterolemia can determine more than 60% of the variability of the frequency of leukemia. At the same time, the level of total Energy does not significantly affect the incidence of leukemia. The ratio and origin of food and macronutrients have a greater effect on the incidence of leukemia than the absolute amounts of food and macronutrients in the nutritional structure.

## Keywords

Risk factors for leukemia, Quality of life, Metabolic syndrome, Obesity, Nutrition structure, Calorie content, Animal and plant products, Alcohol

## Abbreviations

**IR:** Incidence Rate; **QOL:** Quality of Life; **MS:** Metabolic Syndrome; **NS:** Nutrition Structure; **AP:** Animal Products; **CV:** Cereals and Vegetables; **FS:** Fruits and Sweeteners; **AB:** Alcoholic Beverages; **MC:** Mediterranean Countries

## Introduction

Leukemia, or cancer of the hematopoietic system, is a malignant transformation of leukocytes, which prevents the completion of blood cells differentiation [1]. As a result, leukocytes lose their ability to perform their functions, but continue to divide intensively, displacing healthy blood cells, penetrate into the lymph nodes, spleen, pancreas and other organs, causing failures in them [1]. In 2011, cancer deaths in the world were 94.98 for men and 63.33 for women per 100,000 people [2]. In 2018, 2.60% of all cancer patients in the world have leukemia [3]. The acute form of leukemia does not turn into chronic, these are two independent forms. Children are more likely to have acute leukemia, while adults predominantly have chronic leukemia. Acute lymphoblastic leukemia accounts for more than 40% of all oncological children diseases [4]. Risk factors for leukemia are not significantly different from other types of cancer: environmental pollution, including carcinogens, pesticides, ionizing and ultraviolet radiation, alcohol, viral infections, lowering immunity, dietary disorders, overweight and obesity [1, 5]. The mechanisms of interaction of factors causing leukemia are not fully understood [5]. A number of mutations have been identified, including the *Pax5* deletion gene, which causes the replacement of the amino acid lysine with serine in the protein, accompanied by a predisposition to leukemia [6]. In recent years, the survival rate of children with acute leukemia has increased to 90% [7]. However, for 70% of children who survived after leukemia, in subsequent years of life there is a risk of overweight and obesity [8]. The etiology and pathogenesis of this phenomenon are being intensively studied, since overweight and obesity, in turn, increase the risks of cardiovascular diseases, type 2 diabetes and some types of cancer [9]. Research in Seven Countries (Europe and the Mediterranean) showed that the key to preventing the development of chronic diseases is not a reduction in diet, or lowering serum cholesterol, but control of systemic inflammation caused by several factors, including Platelet Activation Factor (PAF), which leads to an increase of cholesterol level [10]. It is suggested that the instrumental effects on the body and head (CRT) of patients during the treatment of leukemia cause overweight and obesity for children. It is believed that these effects affect the hypothalamic centers of regulation of metabolism and eating behavior [11]. As a means of preventing and treating obesity as well as reducing the risk of Non-infectious Chronic Diseases (NCD), various diets are being studied, including the Mediterranean diet (Med Diet) [12-14]. It has been shown that Med Diet during pregnancy and breastfeeding reduces the risk of children acute leukemia and subsequent metabolic disturbance [15].

The purpose of the study is the analysis of leukemia risk factors in 2 groups of Mediterranean Countries (MC), which differ in the frequency of leukemia: 9.9 ± 1.80 versus 4.8 ± 1.30 people/100 thousand (p = 0.002) (2008). The aim is a comparative study of Quality of Life (QOL), Nutrition Structure (NS) and predictors of Metabolic Syndrome (MS) in 14 MC countries: Israel, France, Croatia, Malta, Italy, Lebanon, Spain (Group 1); Turkey, Syrian Arab Republic, Tunisia, Egypt, Libya, Algeria, Morocco (Group 2).

## Materials and Method

Study design is observational statistical analysis.

For this study, we formed a database of leukemia incidence for 14 Mediterranean countries. Leukemia: codes in ICD-10-C91 (Lymphocytic leukemia), C92 (Myeloid leukemia).

Information on the incidence rates (IR) of men's leukemia in 14 countries, standardized by sex and age per 100 thousand people, was selected from the GLOBOCAN database for 2008 [16].

Group 1: 9.9 ± 1.80 people/100 thousand standardized by age: Israel- 13.4, France- 10.2, Croatia- 9.9, Malta- 9.9, Italy- 9.8, Lebanon- 8.4, Spain- 8.2.

Group 2: 4.8 ± 1.30 people/100 thousand standardized by age: Turkey- 5.8, Syrian Arab Republic- 5.1, Tunisia- 4.9, Egypt- 4.8, Libya- 4.4, Algeria- 3.8, Morocco- 2.5.

A number of indicators were used to characterize the Quality of Life (QOL) in the countries: per capita income, or Gross Domestic Product (GDP) for 2008 [17]; the geographical position of countries in terms of latitude and the level of ultraviolet radiation in the capital of the country (UV) [18]; life expectancy for men (LE) [19]; Access to a good health service, clean water and clean air [20]; Happiness Index (HI), or Gross Internal Happiness 2016 [21].

As predictors of Metabolic Syndrome (MS), we studied Body Mass Index (BMI) ≥ 25 $kg/m^2$ and ≥ 30 $kg/m^2$, the percentage of men with overweight and obesity in a country; as well as the percentage of residents with blood cholesterol (Chl) ≥ 5.0 mmol/L and ≥ 6.2 mmol/L [22].

The level of daily food consumption (g/person/day) (53 products) for each country was selected from the FAO database for 1990-2002 and 2003-2005 [23]. The Nutrition Structure (NS) of the countries is presented in the form of 4 blocks in absolute and percentage terms of daily consumption: 1- products of animal origin (AP); 2- Cereals and Vegetables (CV); 3- Fruits and Sweeteners (FS); 4- Alcoholic Beverages (AB) [24]. The composition, ratio, and origin of macronutrients (energy, proteins, fats, and carbohydrates) for 199-2002 and 2003-2005 were also analyzed [23].

Statistical analysis of the results was carried out using: Spearman correlation analysis, Mann-Whitney-Wilcoxon U-test and linear regression analysis for independent samples. U is the numerical value of the Mann-Whitney criterion.

The central trend in the distribution of data in the sample was represented by Median (Me). The variance of the data in the samples was estimated using the Inter Quartile Range (QR) between the first and third quartiles, that is, between the $25^{th}$ and $75^{th}$ percentiles.

Using multiple or paired regression analysis, we assessed the influence of the frequencies of QOL, MS and NS indicators in countries on the incidence of leukemia. The dependent variable was age-standardized IR of leukemia, the independent variables were the frequencies of QOL, MS and NS. The quality of the regression model was assessed using the correlation coefficient (R), the determination coefficient (R2), the F distribution, t-criteria for the regression coefficients and residual analysis. Residues in all models had a normal distribution. An analysis of the values and signs of the coefficients of the regression equations b* and b made it possible to evaluate the contribution of the predictors to the level of leukemia (IR), and using the coefficients b to forecast the effect on the dependent variable when independent variables were changed per unit of measure, statistically significantly related to the IR of the dependent variable. The essence of the regression analysis was to find the most important factors that influenced on the dependent variable (leukemia frequency).

The level of statistical significance P reflected the degree of accuracy of the conclusion about the differences between indicators of groups of countries 1 and 2. Two levels of accuracy were evaluated: 1: $p \le 0.01$- error probability of 1%; 2: $p \le 0.05$- error probability of 5%. All calculations were performed using the StatSoft program (version 13).

## Results

### Spearman's correlation analysis of the relationship between short term leukaemia and the studied indicators of quality of life, metabolic syndrome and nutritional structure

As a result of studies, it was found that the tightest correlation ($r > 0.75$; $p < 0.01$) was observed between leukemia IR and per capita income, access to good health service, clean water, blood cholesterol, % of vegetable products, % energy and proteins of macronutrients of animal origin, as well as complete carbohydrates. In addition, a correlation was found ($r > 0.75$; $p < 0.01$) between a short-term leukemia and levels of consumption of certain food products: beef, cheese and coffee (Table 1). The association of short term leukemia with the rest of the studied parameters was lower than Spearman's correlation coefficient 0.75, or had no statistically significant connection.

**Table 1:** Spearman's correlation analysis of the relation of leukemia incidence to environmental factors N = 14, p < 0.05.

| Indicators | Spearman rank order correlations / marked correlations are significant at p <,05000 | | | |
|---|---|---|---|---|
| | Valid | Spearman | t(N-2) | p-value |
| **Indicators of "quality of life"** | | | | |
| GDP $ person/day | 14 | 0.752 | 3.958 | 0.002 |
| UV rad J/m² | 14 | -0.55 | -2.282 | 0.042 |
| Access to the street. Medicine | 14 | 0.796 | 4.552 | 0.001 |
| HPI 2016 | 14 | 0.565 | 2.375 | 0.035 |
| **Dietary pattern** | | | | |
| Total (TCL)-g/person/day 100% | 14 | 0.741 | 3.828 | 0.002 |
| % AP | 14 | 0.691 | 3.31 | 0.006 |
| % GV | 14 | -0.763 | -4.095 | 0.001 |
| % FD | 14 | 0.38 | 1.423 | 0.18 |
| % AB | 14 | 0.772 | 4.211 | 0.001 |
| **General macronaturents** | | | | |
| Energy (kcal/person/day)2003-2005 | 14 | 0.509 | 2.047 | 0.063 |
| Carbohydrate% total Energy | 14 | -0.765 | -4.114 | 0.001 |
| Proteins% total Energy | 14 | 0.601 | 2.604 | 0.023 |
| Fats% total Energy | 14 | 0.727 | 3.672 | 0.003 |
| **Macronaturents of animal products** | | | | |
| AP Energy% total Energy | 14 | 0.835 | 5.249 | 0 |
| AP Protein% total Protein | 14 | 0.835 | 5.253 | 0 |
| AP Fat% total Fat | 14 | 0.706 | 3.45 | 0.005 |
| **Metabolic syndrome** | | | | |
| BMI > 25 (kg/m²) | 14 | 0.638 | 2.871 | 0.014 |
| BMI > 30 (kg/m²) | 14 | 0.612 | 2.678 | 0.02 |
| Ch > 5.0 (mmol/L) | 14 | 0.864 | 5.955 | 0 |
| Ch > 6.2 (mmol/L) | 14 | 0.846 | 5.488 | 0 |
| **Animal products** | | | | |
| Bovine Meat | 14 | 0.762 | 4.078 | 0.002 |
| Cheese | 14 | 0.822 | 5.009 | 0 |
| Fats, animals, raw | 14 | 0.688 | 3.287 | 0.006 |
| Freshwater fish | 14 | 0.641 | 2.896 | 0.013 |
| **Product of plant origin** | | | | |
| Apples | 14 | 0.717 | 3.56 | 0.004 |
| Coffee | 14 | 0.771 | 4.188 | 0.001 |
| Beverages, alcoholic | 14 | 0.659 | 3.038 | 0.01 |
| Wine | 14 | 0.719 | 3.588 | 0.004 |
| Beer | 14 | 0.737 | 3.778 | 0.003 |
| **Relationship of some chronic diseases to GDP$** | | | | |
| Leukemia and GDP $ | 159 | 0.687 | 11.833 | 0 |
| Ischemic heart disease and GDP $ | 159 | -0.318 | -4.195 | 0 |
| Hypertensive heart disease and GDP $ | 159 | -0.394 | -5.367 | 0 |
| Cerebrovascular disease and GDP $ | 159 | -0.62 | -9.913 | 0 |
| Prostate and GDP $ | 159 | 0.593 | 9.23 | 0 |
| Alzheimer and GDP $ | 159 | 0.591 | 9.178 | 0 |
| Parkinson disease and GDP | 159 | 0.348 | 4.656 | 0 |
| Bipolar disorder and GDP $ | 159 | -0.707 | -12.512 | 0 |
| Alcohol use disorder and GDP $ | 159 | 0.419 | 5.783 | 0 |
| Diabetes m and GDP $ | 159 | -0.335 | -4.46 | 0 |

GDP- Domestic Gross Product, BMI- Body Mass Index, Ch- Cholesterol, TCL- Total Daily Consumption Level, AP- Animal Products, GV- Plant-based Products, FS- Fruit and Sweeteners, AB- Alcoholic Beverages, MR- Human Morbidity Rate/100,000 population, DALY- Disability-Adjusted Life Year

### Analysis of the quality of life in Mediterranean countries with a high and low incidence of leukaemia using the Mann-Whitney test

The countries were divided into 2 groups depending on IR of men's leukemia.

Group 1: 9.9 ± 1.80 people/100 thousand standardized by age: Israel- 13.4, France- 10.2, Croatia- 9.9, Malta- 9.9, Italy-

9.8, Lebanon- 8.4, Spain- 8.2. Group 2: 4.8 ± 1.30 people/100 thousand standardized by age: Turkey- 5.8, Syrian Arab Republic- 5.1, Tunisia- 4.9, Egypt- 4.8, Libya- 4.4, Algeria- 3.8, Morocco- 2.5.

In 2008, per capita income (GDP) in the 1st group of countries was 4 times higher than in the 2nd group of countries ($p = 0.005$) (Table 2). The countries of group 1 are located on 5° north latitude higher than the countries of group 2 ($p = 0.2$). The ultraviolet radiation (UV) at these latitudes of the 1st group is 7 J/m² lower than for the 2nd group of countries ($p = 0.03$). In countries of the 1st group, men's leukemia IR was 2 times higher than in countries of the 2nd group ($p = 0.002$). In countries of the 1st group, in comparison with the 2nd group of countries, access to a good health care was 1.3 times higher ($p = 0.002$); access to clean water was 1.2 times higher ($p = 0.006$); and access to clean air was significantly higher (by the coefficient of total child mortality) ($p = 0.008$); life expectancy for men was 7 years higher ($p = 0.021$). The Happiness index (HI) in the 1st group of countries was 1.2 times higher than in the countries of the 2nd group ($p = 0.03$) (Table 2).

Thus, in countries of the 1st group with a higher IR of short-term leukemia, quality of life was statistically significantly higher than in the 2nd group of countries. The highest accuracy of differences in indicators ($p = 0.002$) between countries of the 1st and the 2nd group was in terms of leukemia IR (Table 2).

### Analysis of metabolic syndrome predictors in countries of the 1st and the 2nd groups

In countries of the 1st group, number of men with a BMI > 25 kg/m² was 1.1 times higher than in countries of the 2nd group ($p = 0.011$); with a BMI > 30 kg/m² it was 1.2 times higher than in group 2 ($p = 0.02$); there were 1.5 times more men with serum cholesterol (Chl) > 5.0 mmol/l, ($p = 0.002$); 2.0 times more men with (Chl) > 6.20 mmol/L than in countries of the 2nd group ($p = 0.002$) (Table 2).

Thus, in countries of group 1, the signs of MS in the population are statistically significantly higher than in group 2 of countries.

### Analysis of nutritional structure in two groups of countries

In countries of group 1, the level of Total Daily Consumption (TDC) was 1.3 times higher than in countries of group 2 ($p = 0.005$). In countries of the 1st group, the share of Animal Products (AP) in daily consumption was 1.4 times higher than in countries of the 2nd group ($p = 0.015$). The share of plant products in daily consumption (cereals and vegetables) in countries of group 1 was 1.3 times lower than in countries of group 2 ($p = 0.003$). The share of Fruits and Sweeteners (FS) in daily consumption in the countries of groups 1 and 2 did not statistically differ ($p = 0.20$). The share of Alcoholic Beverages (AB) in daily consumption in the countries of the 1st group was 11 times higher than in the countries of the 2nd group ($p = 0.003$).

Thus, in the 1st group of countries the level of total daily consumption, as well as the consumption of AP, FS and AB was higher than in the 2nd group of countries. At the same time, the percentage of CV products in daily consumption was higher in the 2nd group of countries. The higher accuracy of the difference between the 1st and 2nd group of countries was in terms of consumption of the share of CV and AB in the daily consumption.

### Analysis of the structure of the macronutrients in two groups of countries

#### Structure of full energy

The level of total daily energy in countries of groups 1 and 2 did not statistically differ in 1990-02 and 2003-05 ($p = 0.104$). The level of complete carbohydrates in countries of group 1 was 1.2 times (1990-02) and 1.3 times (2003-05) lower than in countries of group 2 ($p = 0.003$). The level of complete proteins in the 1st and 2nd group of countries did not statistically differ between the groups of countries over the 15-year period ($p = 0.1$). At the same time, the level of fats in group 1 was 1.4 times higher than in group 2 at both follow-up periods of 15 years ($p = 0.006$).

Thus, the level of full energy, as well as proteins in the countries of groups 1 and 2 was the same, and did not change significantly over the 15-year period. However, the level of carbohydrates in the 1st and 2nd group of countries decreased by 5% and 3% over 15 years. The level of fats was 1.4 times higher in group 1 than in group 2 in both periods of observation. But the level of fats in the 1st and 2nd group of countries increased by 5% and 3% over 15 years, respectively. However, these changes were not statistically significant (Table 2).

### Analysis of the structure of macronutrients of animal products

In the countries of the 1st group, the share of energy of animal products in the total energy was 2.4 times higher than in the countries of the 2nd group ($p = 0.002$) in 1990-02, and in 2003-05 ($p = 0.002$). The share of animal proteins in total proteins in countries of group 1 was 2.0 times higher than in countries of group 2: ($p = 0.003$) in 1990-02 and in 2003-05 ($p = 0.002$). The proportion of animal fats in total fats in countries of group 1 was 1.7 times higher than in countries of group 2 in both periods of observation: ($p = 0.003$) and ($p = 0.005$) (Table 2).

Thus, in the 1st group of countries, compared with the 2nd group, the level of energy is 2.4 times higher, the level of proteins is 2 times higher and the level of fats is 1.7 times higher, both in 1990-02 and in 2003-05. The level of macronutrients of daily consumption in the 1st and 2nd group of countries did not statistically significantly change in 15 years.

### Analysis of consumption levels of individual food products in countries of groups 1 and 2

#### Animal products

The level of daily consumption in the 1st group of countries was 1.3 times higher than in the 2nd group ($p = 0.005$) (Table 2).

In countries of group 1, the average daily consumption of meat, dairy and fish products was on average 2.7 times higher than in countries of group 2. However, for individual products, the differences between groups of countries were significant. Beef was 3.4 times ($p = 0.005$); pork was 20 times ($p = 0.011$);

**Table 2:** Comparative analysis of indicators for 1st and 2nd group of countries (Mann-Whitney criterion $p \geq 0.05$) N = 7/7, $p < 0.05$.

| Indicators | U | Z | p-value | Valid N1 | Median 1 | Quartile 1 | Valid N2 | Median 2 | Quartile 2 |
|---|---|---|---|---|---|---|---|---|---|
| IR Leukemia | - | 3.07 | 0.002 | 7 | 9.9 | 1.8 | 7 | 4.8 | 1.3 |
| M DALY | 6 | -2.3 | 0.021 | 7 | 10801 | 4200.2 | 7 | 17271 | 1403.9 |
| M death | 6 | -2.3 | 0.021 | 7 | 607 | 329.6 | 7 | 938 | 41.1 |
| GDP $ person/day | 2 | 2.81 | 0.005 | 7 | 29 | 15.8 | 7 | 7 | 8 |
| Lat° | 14 | 1.28 | 0.201 | 7 | 40 | 11.8 | 7 | 35 | 4.1 |
| UV rad J/m$^2$ | 7 | -2.17 | 0.03 | 7 | 2705 | 1115 | 7 | 3501 | 608 |
| Prosperity rating | 5 | -2.43 | 0.015 | 7 | 37 | 30 | 7 | 96 | 32 |
| Rating. educations | 4 | -2.56 | 0.011 | 7 | 41 | 28 | 7 | 86 | 23 |
| Health | 1 | -2.94 | 0.003 | 7 | 25 | 17 | 7 | 73 | 21 |
| Access to the street. medicine | - | 3.07 | 0.002 | 7 | 100 | 0 | 7 | 85 | 20 |
| Access to clean water | - | 2.76 | 0.006 | 7 | 100 | 0 | 7 | 84 | 17 |
| Air pollution for children under 5 years old | 2 | -2.64 | 0.008 | 7 | 0 | 1 | 7 | 46 | 104 |
| Male life expectancy | 6 | 2.3 | 0.021 | 7 | 77 | 5.7 | 7 | 70 | 4.6 |
| Index of human development | 2 | 2.81 | 0.005 | 7 | 1 | 0.1 | 7 | 1 | 0.1 |
| Ecological Efficiency Index (EEI) | 9 | 1.92 | 0.055 | 7 | 66 | 21.3 | 7 | 55 | 8.9 |
| Index of Happiness (HPI) | 7 | 2.17 | 0.03 | 7 | 6.361 | 1 | 7 | 5.151 | 1.3 |
| **Metabolic syndrome** | | | | | | | | | |
| BMI ≥ 25 (kg/m$^2$) | 4 | 2.56 | 0.011 | 7 | 64 | 5.9 | 7 | 58 | 18.3 |
| BMI ≥ 30 (kg/m$^2$) | 6 | 2.3 | 0.021 | 7 | 24 | 5.3 | 7 | 20 | 10.9 |
| ch ≥ 5.0 (mmol/L) | - | 3.07 | 0.002 | 7 | 59 | 13.2 | 7 | 37 | 3.5 |
| ch ≥ 6.2 (mmol/L) | - | 3.07 | 0.002 | 7 | 17 | 6.7 | 7 | 7 | 1.3 |
| **Dietary pattern** | | | | | | | | | |
| | | | | | *185* | | | *8* | |
| TCL g/person/day | 2 | 2.81 | 0.005 | 7 | 2244 | 427 | 7 | 1701 | 186 |
| % AP | 5 | 2.43 | 0.015 | 7 | 30 | 6.2 | 7 | 22 | 11.3 |
| % GV | 1 | -2.94 | 0.003 | 7 | 49 | 13.1 | 7 | 66 | 8.5 |
| % FD | 14 | 1.28 | 0.201 | 7 | 12 | 2.3 | 7 | 11 | 3 |
| % AB | 1 | 2.94 | 0.003 | 7 | 9 | 11 | 7 | 1 | 0.7 |
| **General macronaturents** | | | | | | | | | |
| Energy (kcal/person/day) 1990-1992 | 9 | 1.64 | 0.1 | 7 | 3390 | 300 | 7 | 3140 | 370 |
| Energy (kcal/person/day) 2003-2005 | 12.5 | 1.47 | 0.142 | 7 | 3540 | 450 | 7 | 3190 | 300 |
| Carbohydrate% energy 1990-1992 | 1 | -2.94 | 0.003 | 7 | 55 | 13 | 7 | 66 | 9 |
| Carbohydrate% energy 2003-2005 | 1.5 | -2.87 | 0.004 | 7 | 50 | 13 | 7 | 63 | 11 |
| Proteins% energy 1990-1992 | 12.5 | 1.47 | 0.142 | 7 | 13 | 3 | 7 | 11 | 1 |
| Proteins% energy 2003-2005 | 10.5 | 1.72 | 0.085 | 7 | 13 | 2 | 7 | 11 | 0 |
| Fats% energy 1990-1992 | 1.5 | 2.87 | 0.004 | 7 | 32 | 9 | 7 | 23 | 10 |
| Fats% energy 2003-2005 | 2.5 | 2.75 | 0.006 | 7 | 37 | 11 | 7 | 26 | 12 |
| **Macronaturents of animal products** | | | | | | | | | |
| AP energy% energy 1990-1992 | - | 3.07 | 0.002 | 7 | 26 | 7 | 7 | 11 | 6 |
| AP energy% energy 2003-2005 | - | 3.07 | 0.002 | 7 | 26 | 7 | 7 | 10 | 4 |
| AP protein% protein 1990-1992 | 1 | 2.94 | 0.003 | 7 | 53 | 9 | 7 | 25 | 8 |
| AP protein% protein 2003-2005 | - | 3.07 | 0.002 | 7 | 54 | 15 | 7 | 26 | 9 |
| AP Fat% fat 1990-1992 | 1 | 2.94 | 0.003 | 7 | 47 | 23 | 7 | 28 | 3 |
| AP Fat% fat 2003-2005 | 2 | 2.81 | 0.005 | 7 | 44 | 27 | 7 | 26 | 10 |
| Total (TCL)- g/person/day2003-05 | 2 | 2.81 | 0.005 | 7 | 2244 | 427 | 7 | 1701 | 186 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Animal products** | | | | | | | | | |
| Bovine meat | 1 | 2.94 | 0.003 | 7 | 60 | 25 | 7 | 14 | 8 |
| Pig meat | 4 | 2.56 | 0.011 | 7 | 90 | 110 | 7 | 3 | 32 |
| Mutton and goat meat | 9 | -1.92 | 0.055 | 7 | 5 | 5 | 7 | 16 | 8 |
| Poultry meat | 5 | 2.43 | 0.015 | 7 | 64 | 34 | 7 | 33 | 10 |
| Offals, edible | 7 | 2.17 | 0.03 | 7 | 7 | 15 | 7 | 3 | 3 |
| Meat, other | - | 3.07 | 0.002 | 7 | 43 | 8 | 7 | 21 | 9 |
| Milk, whole | 18.5 | 0.7 | 0.482 | 7 | 194 | 153 | 7 | 188 | 192 |
| Milk, skimmed | 23 | 0.13 | 0.898 | 7 | 36 | 80 | 7 | 46 | 56 |
| Eggs | 4.5 | 2.49 | 0.013 | 7 | 32 | 13 | 7 | 19 | 12 |
| Cheese | 2 | 2.81 | 0.005 | 7 | 34 | 44 | 7 | 5 | 13 |
| Fish amount | 5.5 | 2.36 | 0.018 | 7 | 60 | 46 | 7 | 25 | 22 |
| Animal origin mkg | - | 3.07 | 0.002 | 7 | 4 | 2.5 | 7 | 2 | 0.3 |
| Fats, animals, raw | 3 | 2.68 | 0.007 | 7 | 9 | 12 | 7 | 1 | 1 |
| AP amount | 4 | 2.56 | 0.011 | 7 | 664 | 193 | 7 | 413 | 216 |
| **Vegetal products** | | | | | | | | | |
| Wheat | 4 | -2.56 | 0.011 | 7 | 323 | 129 | 7 | 497 | 154 |
| Coffee | 0.5 | 3 | 0.003 | 7 | 13 | 3 | 7 | 2 | 1 |
| Potatoes | 4 | 2.56 | 0.011 | 7 | 193 | 97 | 7 | 86 | 76 |
| Tomatoes | 15 | -1.15 | 0.25 | 7 | 132 | 95 | 7 | 229 | 172 |
| Olive oil | 21.5 | 0.32 | 0.749 | 7 | 4 | 30 | 7 | 5 | 11 |
| Vegetal origin | 19.5 | -0.57 | 0.565 | 7 | 12 | 4.3 | 7 | 13 | 3 |
| **Fruit and sweeteners** | | | | | | | | | |
| Oranges | 6.5 | 2.24 | 0.025 | 7 | 78 | 51 | 7 | 56 | 36 |
| Lemons, limes | 13.5 | 1.34 | 0.18 | 7 | 19 | 22 | 7 | 8 | 8 |
| Apples | 7.5 | 2.11 | 0.035 | 7 | 43 | 10 | 7 | 28 | 21 |
| Sugar (raw equivalent) | 18.5 | 0.7 | 0.482 | 7 | 92 | 26 | 7 | 92 | 28 |
| **Alcoholic beverages** | | | | | | | | | |
| Beverages, alcoholic | 6 | 2.3 | 0.021 | 7 | 7 | 5 | 7 | 0 | 2 |
| Wine | 0.5 | 3 | 0.003 | 7 | 98 | 124 | 7 | 0 | 2 |
| Beer | 2 | 2.81 | 0.005 | 7 | 80 | 173 | 7 | 8 | 11 |
| **Chronic diseases (DALY/100 000)** | | | | | | | | | |
| Ischemic heart disease | 9 | -1.92 | 0.055 | 7 | 645 | 874.6 | 7 | 1834 | 843.6 |
| Hypertensive heart disease | 3 | -2.68 | 0.007 | 7 | 40 | 47.7 | 7 | 342 | 198.4 |
| Cerebrovascular disease | 9 | -1.92 | 0.055 | 7 | 330 | 418.7 | 7 | 669 | 413.8 |
| Alzheimer disease | 2 | 2.81 | 0.005 | 7 | 214 | 33.1 | 7 | 115 | 42.6 |
| Parkinson disease | 6 | 2.3 | 0.021 | 7 | 47 | 13.1 | 7 | 19 | 11.6 |
| Alcohol use disorders | 7 | 2.17 | 0.03 | 7 | 216 | 656 | 7 | 104 | 123.3 |
| Diabetes mellitus | 15 | -1.15 | 0.25 | 7 | 254 | 196.6 | 7 | 417 | 185 |
| Tuberculosis | 1 | -2.94 | 0.003 | 7 | 10 | 22 | 7 | 70 | 67 |

BMI- Body Mass Index, Ch- Cholesterol, TCL- Daily Consumption Level, AP- Animal Products, GV- Plant-based Products, FD- Fruit and Sweeteners, AB- Alcoholic Beverages, E- Total Energy, P- Total Protein, F- Total Fat, IR- Human Morbidity Rate/100,000 population, GDP- Domestic Gross Product, DALY- Disability-Adjusted Life Year poultry meat was 1.5 times (p = 0.015); eggs were 1.5 times (p = 0.013); cheese was 5 times (p = 0.005); fish and seafood were 2 times (p = 0.018); animal fats were 9 times (p = 0.007); iron of animal origin was 2 times higher than in group 2 (p = 0.002).

In total, animal products consumed per day in 1st group of countries was 1.5 times higher than in 2nd group (p = 0.011) (Table 2).

**Analysis of levels of consumption of plant products (CV, FS, AB)**

Cereals and vegetables (CV)

In countries of groups 1 and 2, the levels of average daily consumption of CV had a low severity of differences, both for individual products and in total: in the 2nd group wheat was 1.8 times higher (p = 0.011); rice (p = 0.9); corn (p = 0.18); barley 0 (p = 0.2); beans (p = 0.1); rye (p = 0.8); nuts (p = 0.3). In 1st group of countries potatoes are 2 times higher (p = 0.01); tomatoes (p = 0.3); greenery (p = 0.3); other vegetables (p = 0.1); soybean oil (p = 0.3); sunflower oil (p = 0.1); olive oil (p = 0.8); iron of plant products (p = 0.6).

In total, in the countries of group 2 consumption of cereals and vegetables was 1.2 higher than in group 1, but it is statistically insignificant (p = 0.2) (Table 2).

Fruits and sweeteners

The consumption levels of certain products, with the exception of coffee, in the countries of groups 1 and 2 did not have statistically significant differences (Table 2). Coffee consumption was 5 times higher in group 1 countries (p = 0.003). Total FS consumption in countries of group 1 was 1.5 times higher than in group 2 (p = 0.005) (Table 2).

Alcoholic beverages

The average daily consumption of alcoholic beverages (AB) in the countries of the 1st group was 11 times higher than in the countries of the 2nd group (p = 0.002). Strong spirits consumption in the countries of group 1 was 7 times higher (p = 0.02); wine is 100 times higher (p = 0.003) and beer is 10 times higher than in the 2nd group of countries (p = 0.005) (Table 2).

Thus, the consumption of individual animal products, FS and AB as well as their total amount as a whole was higher in 1st group of countries. The total consumption and consumption of individual CV products differs slightly in the 1st and 2nd group of countries. However, the share of animal products, CV and AB was statistically significantly different for the 1st and 2nd group of countries.

The correlation between the correlation analysis and the U-Mann-Whitney criterion was 96%.

**The results of paired and multiple regression analysis of the influence of independent variables, indicators of quality of life, metabolic syndrome and nutrition structure, on the dependent variable: leukaemia IR**

As a result of studies, it was found that the determination coefficient (R2) in excess of 0.6 was observed in the following independent variables: per capita income, access to clean water, cholesterol > 5.0 mmol/L, total daily consumption of animal products, % of animal Protein, levels of consumption of red meat (Bovine Meat), iron of animal origin, and coffee.

The highest accuracy in predicting of the effect of an independent variable on a dependent variable, short-term leukemia, with a change in b per unit of measure was observed for independent variables: per capita income, cholesterol > 5.0 mmol/L, consumption of animal products, % of animal protein, level of consumption of red meat (Bovine Meat), iron of animal origin, and coffee (Table 3).

Comparison of the results of three statistical methods (Spearman's correlation coefficient, Mann-Whitney U-test, and paired and multiple regression analysis) showed high consistency of research results, which increases the reliability of the identified patterns.

## Discussion

Studies have shown that the characteristics of Quality of Life (QOL), Metabolic Syndrome (MS) and Nutrition Structure (NS) in the 1st group of Mediterranean countries with a leukemia frequency of 9.9 ± 1.80 people/100 thousand had statistically significant differences with countries of the 2nd group with a leukemia frequency of 4.8 ± 1.30 people/100 thousand. Good agreement was obtained between the research results using three statistical methods: Spearman correlation analysis, Mann-Whitney U-test and multiple regression analysis with prediction. At the same time, each of the methods made it possible to obtain additional information in accordance with the tasks. Thus, Spearman's correlation analysis indicated significant associations of risk factors with the incidence of leukemia. The U-Mann-Whitney criterion made it possible to obtain comparative quantitative characteristics of leukemia risk factors in two groups of countries, similar to the case-control method. Regression analysis, in addition to associations, made it possible to assess the quantitative dependence (prognosis) of the frequency of leukemia on risk factors, as well as to determine protective factors. It has been established that the frequency of men's leukemia in Mediterranean countries is the higher, the higher the per capita income (GDP); Human Development Index (HDI); Happiness Index (HI); access to a good health care, clean water, clean air; life expectancy, and the lower total mortality. Similar information was obtained for other tumors, including leukemia, in European countries [14]. 64% of men in 1st group of countries, unlike the 2nd group, had overweight (BMI > 25 kg/m$^2$), and 24% had obesity (BMI > 30 kg/m$^2$) (p = 0.01). 76% of men in the 1st group of countries, unlike the 2nd group, had hypercholesterolemia (Chl > 5.0 and > 6.2 mmol/L) (p = 0.02). The indicators of MS for the 1st of the Mediterranean group of countries were similar to European countries [14].

It is known that in countries with high and medium incomes, the proportion of people with overweight and obesity began to increase in the second half of the 20th century [25-28]. It is estimated that 20% of cancer cases are associated with over-nutrition and low physical activity [27, 28]. Potential cancer initiators in view of obesity are distinguished: insulin,

**Table 3:** Results of linear paired and multiple regression analysis N = 14, p < 0.05.

| **N=14 Pair regression analysis** | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Dependent variable** | **Independent variables** | **b*** | **R2** | **B** | **F(1,12)** | **t(12)** | **p-value** | **Predicted %** | **Predicted %** | **Predicted IR** |
| IR Leukemia | GDP $ person/day 2008 | 0.801 | 0.641 | 0.23 | 21.44 | 4.63 | 0.0006 | 103.2% | 7.449 | IR Leukemia |
| IR Leukemia | HPI 2016 | 0.592 | 0.233 | 1.78 | 0.7 | 2.55 | 0.0256 | 125.0% | 9.006 | IR Leukemia |
| IR Leukemia | % AP | 0.729 | 0.531 | 0.33 | 13.6 | 3.69 | 0.0031 | 104.6% | 7.556 | IR Leukemia |
| IR Leukemia | % GV | -0.762 | 0.581 | -0.21 | 16.64 | -4.08 | 0.0015 | 97.1% | 7.015 | IR Leukemia |
| IR Leukemia | % AB | 0.586 | 0.344 | 0.33 | 6.29 | 6.6 | 0.0275 | 104.6% | 7.556 | IR Leukemia |
| IR Leukemia | % Fish | 0.565 | 0.319 | 1.65 | 5.62 | 2.37 | 0.0353 | 122.8% | 8.869 | IR Leukemia |
| IR Leukemia | % Oil | 0.284 | 0.081 | 1.16 | 1.05 | 1.03 | 0.3247 | 116.0% | 8.382 | IR Leukemia |
| IR Leukemia | Total (TCL)- g/ person/day | 0.757 | 0.573 | 0.01 | 16.08 | 4.01 | 0.0017 | 100.1% | 7.229 | IR Leukemia |
| IR Leukemia | AP amount | 0.784 | 0.614 | 0.01 | 19.09 | 4.37 | 0.0009 | 100.2% | 7.234 | IR Leukemia |
| IR Leukemia | GV amount | -0.248 | 0.061 | -0.01 | 0.78 | -0.89 | 0.3934 | 99.9% | 7.22 | IR Leukemia |
| IR Leukemia | FD amount | 0.737 | 0.543 | 0.05 | 6.29 | 3.77 | 0.0026 | 100.7% | 7.268 | IR Leukemia |
| IR Leukemia | AB amount | 0.596 | 0.355 | 0.015 | 6.6 | 2.57 | 0.0246 | 100.2% 1% | 7.237 | IR Leukemia |
| IR Leukemia | Fish amount | 0.631 | 0.398 | 0.07 | 7.93 | 2.82 | 0.0156 | 101.0% | 7.295 | IR Leukemia |
| IR Leukemia | Oil amount | 0.444 | 0.197 | 0.08 | 2.95 | 1.72 | 0.1114 | 101.1% | 7.299 | IR Leukemia |
| IR Leukemia | Energy (kcal/person/ day)2003-2005 | 0.592 | 0.35 | 0.01 | 6.48 | 2.54 | 0.0257 | 100.1% | 7.229 | IR Leukemia |
| IR Leukemia | Carbohydrate% E 2003-2005 | -0.774 | 0.599 | -0.28 | 15.83 | -4.23 | 0.0012 | 96.2% | 6.946 | IR Leukemia |
| IR Leukemia | Proteins% E 2003-2005 | 0.662 | 0.438 | 1.72 | 9.37 | 3.06 | 0.0099 | 124.0% | 8.945 | IR Leukemia |
| IR Leukemia | Fats% E 2003-2005 | 0.754 | 0.569 | 0.29 | 0.073 | 3.98 | 0.0018 | 104.0% | 7.513 | IR Leukemia |
| IR Leukemia | Male BMI > 30($kg/m^2$) | 0.666 | 0.444 | 0.37 | 9.57 | 3.09 | 0.0093 | 105.2% | 7.594 | IR Leukemia |
| IR Leukemia | Maletch > 6.2(mmol/L) | 0.762 | 0.581 | 0.42 | 16.66 | 4.08 | 0.0015 | 105.9% | 7.644 | IR Leukemia |
| IR Leukemia | AP Energy% 2003-2005 | 0.798 | 0.637 | 0.29 | 21.03 | 4.59 | 0.0006 | 104.0% | 7.509 | IR Leukemia |
| IR Leukemia | AP Protein% 2003-2005 | 0.857 | 0.735 | 0.17 | 33.26 | 5.77 | 0.0001 | 102.3% | 7.389 | IR Leukemia |
| IR Leukemia | AP Fat% 2003-2005 | 0.636 | 0.405 | 0.16 | 8.16 | 2.86 | 0.0145 | 102.2% | 7.377 | IR Leukemia |
| IR Leukemia | Diversification dietary Energy% | 0.809 | 0.655 | 0.2 | 22.76 | 4.77 | 0.0005 | 102.8% | 7.421 | IR Leukemia |
| IR Leukemia | Animal origin 2003-2005 | 0.815 | 0.664 | 1.64 | 23.76 | 4.87 | 0.0004 | 123.0% | 8.863 | IR Leukemia |
| IR Leukemia | UV rad $J/m^2$ 2004 | -0.497 | 0.247 | 0 | 3.95 | -1.99 | 0.0703 | 100.0% | 7.219 | IR Leukemia |
| IR Leukemia | Bovine meat 2003-2005 | 0.826 | 0.683 | 0.11 | 25.87 | 5.09 | 0.0003 | 101.5% | 7.328 | IR Leukemia |
| IR Leukemia | Beverages, alcoholic 2003-2005 | 0.681 | 0.464 | 0.62 | 10.38 | 3.22 | 0.0073 | 108.7% | 7.846 | IR Leukemia |
| **N=14 Multiple regression analysis** | | **b*** | | **B** | | **t(12)** | **p-value** | **Predicted %** | **Predicted MR Leukemia** | |
| **Quality of life** | | | | | | | | | | |
| IR Leukemia | IHD (9 Independent variables) | 0.835 | 0.697 | 26.64 | 20.661 | 4.545 | 0.0014 | 100.4% | 7.25 | IR Leukemia |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| DALY Ischemic heart disease the quality of life | GDP $ (2 Independent variables) | -0.730 | 0.533 | -49.298 | 13.695 | -3.701 | 0.003 | 96.6% | 1373 | DALY Ischemic heart disease the quality of life |
| DALY Hypertensive heart disease | GDP $ (2 Independent variables) | -0.744 | 0.553 | -11.729 | 14.841 | -3.852 | 0.002 | 93.8% | 182 | DALY Hypertensive heart disease |
| DALY Cerebrovascular disease | GDP $ (2 Independent variables) | -0.823 | 0.464 | -25.631 | 4.756 | -3.068 | 0.011 | 95.9% | 609 | DALY Cerebrovascular disease |
| **Metabolic syndrome** | | | | | | | | | | |
| IR Leukemia | Maletch > 6.2(mmol/L) (7 Independent variables) | 0.868 | 0.753 | 0.362 | 24.351 | 4.935 | 0.0011 | 104.8% | 7.568 | IR Leukemia |
| **Dietary patterns** | | | | | | | | | | |
| IR Leukemia | % GV (4 Independent variables) | -0.762 | 0.581 | -0.207 | 16.638 | -4.079 | 0.0015 | 97.2% | 7.015 | IR Leukemia |
| **Macronutrients of animal products** | | | | | | | | | | |
| IR Leukemia | AP Protein% (3 Independent variables) | 0.857 | 0.735 | 0.168 | 33.264 | 5.767 | 0.0001 | 102.3% | 7.389 | IR Leukemia |
| **General macronutrients** | | | | | | | | | | |
| IR Leukemia | Fats % Energy (3 Independent variables) | 0.754 | 0.569 | 0.291 | 15.834 | 3.979 | 0.0018 | 104.0% | 7.513 | IR Leukemia |
| **Micronutrients** | | | | | | | | | | |
| IR Leukemia | animal origin (3 Independent variables) | 0.815 | 0.664 | 1.642 | 23.759 | 4.874 | 0.0004 | 102.3% | 7.386 | IR Leukemia |
| **Diversification dietary pattern** | | | | | | | | | | |
| IR Leukemia | Proteins % (3 Independent variables) | 0.862 | 0.743 | 0.185 | 34.731 | 5.893 | 0.0001 | 102.6% | 7.409 | IR Leukemia |

R2- Determination Coefficient $ BMI- Body Mass Index, Ch- Cholesterol, TCL- Daily Consumption Level, AP- Animal Products, GV- Plant-based Products, FD- Fruit and Sweeteners, AB- Alcoholic Beverages, E- Total Energy, P- Total Protein, F- Total Fat, IR- Human Morbidity Rate/100,000 population, DALY- Disability-Adjusted Life Year, IHD- Index of Human Development, GDP- Domestic Gross Product

insulin-like growth factor-I, sex steroids and adipokines [25-27]. New mechanisms of cancer initiation have been proposed: chronic inflammation, oxidative stress, cross-linking between tumor cells and surrounding adipocytes, migration caused by obesity and hypoxia of adipose stromal cells, and a genetic predisposition [25-28]. At the same time, a decrease in BMI from 40.0 to 18 kg/m$^2$ (bariatric surgery) reduces the risk of cancer, but causes an increased craving for alcohol, which is also a risk factor for cancer and noninfectious chronic diseases [25, 29, 30]. The World Cancer Research Foundation (WCRF) suggests that the average adult BMI should be maintained in the range of 21 to 23 kg/m$^2$ [25, 27]. In addition, it has been shown that environmental cancer risk factors, including leukemia, cause DNA hypermethylation [31].

Mediterranean diet (MedDiet) helps to reduce the risk of chronic diseases, like cancer, including leukemia and acute leukemia [9, 11, 32, 33]. Adults who have had acute leukemia in childhood have a high risk of obesity, hyperlipidemia, cardiovascular diseases, and diabetes mellitus [34-36]. In general, many studies have proven the association of a healthy lifestyle with a decrease in the prevalence of insulin resistance, hypertension, and dyslipidemia [37-39]. The MedDiet reduces the risk of MS by 31% [40]. The violations of the MS established by us in the Mediterranean countries of group 1 are apparently the result of the influence of nutrition structure in these countries. Studies have shown that the total daily food consumption in the 1$^{st}$ group of Mediterranean countries was 1.3 times higher than in the 2$^{nd}$ group ($p = 0.005$). The source of the observed differences in the MS indicators between the 1$^{st}$ and 2$^{nd}$ group of countries was probably the percentage composition of the NS blocks: animal products, CV, FS and AB, which had significant differences between the 1$^{st}$ and 2$^{nd}$ group of countries. Thus, in the 1$^{st}$ group animal products were 30% versus 22% in the 2$^{nd}$ group of countries ($p = 0.015$); CV- 49% versus 66% ($p = 0.003$); AB- 9% against 1% ($p = 0.003$) and FS- 12% against 11% ($p = 0.2$).

However, the daily energy levels (kcal/person/day) in the 1$^{st}$ and 2$^{nd}$ groups of countries did not statistically differ both in 1990-03 and in 2003-05. At the same time, in both periods of observation, the levels of total carbohydrates were

1.1 times lower, and fats 1.4 times higher in the 1st group of Mediterranean countries compared to the 2nd group. In addition, the levels of macronutrients of animal products-energy, proteins and fats were 2.5, 2.1 and 1.7 times higher in the 1st group of countries compared to the 2nd group, both in 1990-03 and in 2003-05. Earlier, we noted similar data for breast cancer and other tumors in European countries [11, 14].

Thus, with the same and sufficiently high total energy in the two groups of countries (3540 and 3190 kcal/person/day p = 0.14), the levels of both total macronutrients and macronutrients of animal origin in the total energy, as well as their ratio, had significant differences between the 1st and 2nd groups of countries. Earlier, the important role of the ratio and origin of macronutrients that make up the total energy was noted [11, 14, 41, 42].

The regression coefficients (b) in the paired regression analysis with an increase of 1% in the characteristics of the independent variables (% AP or % AB) increased the frequency of leukemia by 4.6% (dependent variable) (p = 0.003) and (p = 0.027), respectively, at a confidence interval of ± 95.0%. A 1% increase in the independent variable, % CV, decreased the incidence of leukemia by 2.9% with a confidence interval of ± 95.0% (p = 0.002). This factor can be considered protective. The highest determination coefficients (R2 > 0.60) were found for independent variables: animal proteins (R2 = 0.73 p = 0.0001), iron of animal origin (R2 = 0.66 p = 0.0004), beef (R2 = 0.68 p = 0.0003), energy of AP (R2 = 0.64 p = 0.0006), cholesterol > 5.0 (mmol/L) (R2 = 0.64 p = 0.0006). These factors accounted for more than 60% of the variability in the incidence rate of leukemia in Mediterranean countries. It should be noted that the absolute amount of food consumption and nutrition structure blocks (g/person/day) had a minimal (b- 0.1%) effect on the incidence of leukemia in countries. An increase in calorie content by 1 kcal/person/day increased the incidence of leukemia by 0.1% (R2 = 0.35 p = 0.03). This suggests that the correlation and origin of the levels of consumption of products and macronutrients in the nutrition structure plays a more important role as a risk factor for leukemia.

It was shown that 68% of US residents in 2008 had overweight and obesity [43]. Higher BMI accounted for 18% of leukemia patients [44]. It is believed that metabolic, endocrine, immune and inflammatory changes that occur during obesity can increase the speed of mutations and disrupt DNA repairing, or induce epigenetic changes [45]. Obesity can create an environment in which previously dormant cell clones appear which increase the risk of hematologic cancer [45]. It has been proven that MedDiet reduced the risk of cardiovascular diseases, cancer, and depression [46-48]. However, a cholesterol-lowering diet did not improve mood of patients with high cholesterol levels [49]. A low-fat, high-carbohydrate diet did not improve the quality of life of patients with high risk of cardiovascular diseases [50]. The intervention of a low-fat diet did not change the quality of life of women with high risk of breast cancer [51]. Several studies of the consumption of fish, fruits, vegetables, and nuts have not shown reliable positive associations with the quality of life of subjects [52, 53]. A report by the EAT-Lancet Commission proposed a plant-based planetary reference diet that has a very low (14 g/day) consumption of red meat [54]. In our studies, the levels of consumption of red meat in the 2nd group of Mediterranean countries are close to the data of the EAT-Lancet Commission. However, researchers [54] argue that data of the health risks of red meat are not only unlikely in the light of our evolutionary history, but are far from being supported by reliable scientific evidence, although red meat consumption has declined in recent years in the United States. At November 17, 2010 MedDiet was announced by UNESCO as a guarantee of health and longevity [55].

In population studies [14, 56], we showed that the incidence of many diseases, indicators of quality of life, MS and NS depend on different income per capita and geographical latitude. This complicates the assessment of risk factors. Perhaps the inconsistency of the above literature data is due to the different nature of the factors affecting the studied parameters.

According to Giovanni De Pergola and Franco Silvestris [25], there is still no clear scientific doctrine that preventing weight gain significantly reduces the risk of cancer.

## Conclusion

A study of risk factors for men's leukemia in Mediterranean countries showed that the incidence rate of leukemia is 2 times higher in countries with a higher quality of life, with a higher percentage of men with overweight, obesity and hypercholesterolemia, with a higher level of macronutrients, as well as animal products. Energy and proteins of animal products, beef and iron of animal origin, as well as hypercholesterolemia can determine more than 60% of the variability of the leukemia frequency. The level of total energy does not significantly affect the leukemia incidence rate.

The advantage of the study is that, thanks to the three statistical methods, convincing data were obtained on the effect of overweight and obesity on the leukemia frequency, which are the result of a high content in the nutritional structure of the relative share of animal products and alcoholic beverages.

The disadvantage of the study is that the identified patterns and risk factors for leukemia cannot be used as preventive measures for a specific person. The fact is that in every country in the world, including Mediterranean countries, there is a large number of diseases, more than 220 nosological forms. For example, the burden of cardiovascular diseases is higher, the lower per capita income in countries [56]. At the same time, the frequency of leukemia in countries is higher, the higher the per capita income, as our studies show. Therefore, the nutritional structure in the 1st group of Mediterranean countries is a risk factor for leukemia, but not for cardiovascular diseases. In the 1st group of Mediterranean countries, the burden (DALY per 100 thousand) of cardiovascular diseases is 3-4 times lower than in the 2nd group of countries, in which the incidence of leukemia is 2 times lower than in the 1st group of countries (Table 2 and 3). Therefore, the nutritional structure in the 2nd group of countries with a high relative share of plant products and a low share of alcoholic beverages serves as a protective factor for leukemia, but, apparently, a risk factor for cardiovascular diseases [56]. In every country in the world, disease rates (or DALYs) can be correlated with a positive or negative correlation. Therefore, there cannot be a unified nutritional structure or diet for a specific country. Therefore, neither a country, nor a group of countries can represent a unified "planetary" diet. Apparently, the nutritional structure as a risk factor or as a protective factor, should be unique and determined experimentally. Using of specific diets as the prevention of a disease for a particular person can be determined by his individual genetic predisposition to a particular disease.

## Findings

Overweight, obesity and hypercholesterolemia were important risk factors for an increased incidence rate of leukemia (9.9 ± 1.80) in a number of Mediterranean countries, probably due to the high level of consumption of animal products and alcoholic beverages. A high relative proportion of plant products in the nutrition structure is a protective factor for leukemia.

## Conflicts of Interest

In accordance with the rules of the International Committee of Medical Journal Editors, the authors state that the study was conducted in the absence of any interest.

## Recommendations

The results can be used to diagnose and prevent chronic diseases and prevent obesity.

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