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Association of the Consumption of Milk and Dairy Products with Mortality from Digestive Organs Cancers in Serbia: An Ecological Study †

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Abstract: In this ecological study, correlation between mortality from digestive organs cancers and the per capita consumption of milk and dairy products was assessed using multivariate linear regression analysis (by the β coefficient, with 95% CIs). Milk consumption was independently positively associated with esophageal cancer mortality in men (β = +0.042, 95% CI = 0.003–0.081, p = 0.038). In women, a significant positive association was observed between the consumption of milk and mortality from stomach cancer (β = +0.072, 95% CI = 0.034–0.111, p = 0.002). In contrast, per capita consumption of yogurt, cheese and other dairy products was not independently correlated with mortality from either of the other digestive organs cancers.

Keywords: cancer; digestive organs; dairy; ecological study

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1. Introduction

In recent years, there were more than 6000 digestive cancer deaths (about 3500 males and 2500 females) in Serbia yearly, with unfavorable mortality trends in last decades [1,2].

Although major risk factors for digestive cancers were established, numerous studies suggest that importance of certain dietary factors in etiology of digestive cancers [3,4]. The association between consumption of food and mortality rates from cancer has been found to vary in significance and magnitude across countries [5–7]. Besides, a pooled analysis of 14 cohort studies among 862,680 individuals, showed that there was no association between total milk intake and pancreatic cancer risk, as well as between intakes of low-fat milk, whole milk, cheese, yogurt; findings were consistent within sex [8].

Only a few studies have been done to evaluate the association between the mortality of cancer and food consumption in Serbia [9]. The aim was to assess the relationship between per capita consumption of milk and dairy products and mortality rates for digestive organs cancers.

2. Materials and Methods

This nationwide, ecological study analyzed relationship between per capita consumption of dairy and mortality for digestive cancers in Serbia, for the period 2006–2019.

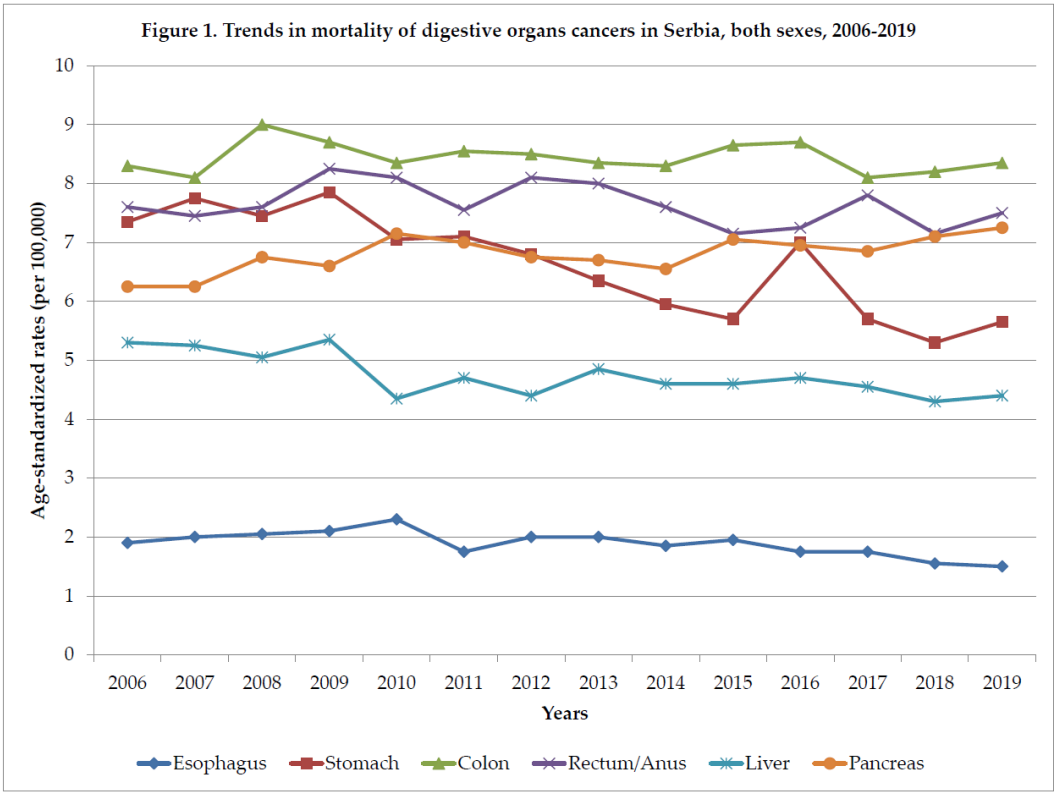
Mortality data and per capita food consumption were obtained from official databases in Serbia (Demographic Statistics and the Household Budget Surveys). The age-standardized mortality rates (for cancer of esophagus, stomach, colon, rectum and anus,

liver and pancreas) were calculated by direct method (Segi's World standard population was used as reference) and were expressed per 100 000 persons. Linear trend models were used to examine trend of mortality from selected cancers. In the Serbian Household Budget Survey the following dairy items were selected: milk, cheese, yoghurt and other products (including butter, cream and sour cream). Food was represented by following units: milk (L), cheese (kg), yoghurt (L), other dairy products (L).

The relationship between mortality rates and consumption of the food was examined by calculating a bivariate correlation coefficient—the Pearson's correlation coefficient (r). In addition, multivariate linear regression analysis was used to assess the strength and direction of the relationship between consumption of dairy and variation in the mortality. In order to control for the influence of gender on the association between consumption of food and mortality rates from cancer, multivariate linear regression analysis was conducted for males and females separately. Multivariate linear regression analysis was used to determine the β coefficient (with 95% CIs, Confidence Intervals). Statistical significance was considered when $p < 0.050$. All statistical analyses were conducted using the Statistical Package for Social Sciences software (v. 20.0, SPSS Inc., Chicago, IL, USA).

3. Results

In Serbia, the markedly decreasing trends in mortality from cancer of esophagus (y = 76.0x − 0.04, $p = 0.004$), stomach (y = 366.7x − 0.18, $p < 0.001$) and liver (y = 136.6x − 0.07, $p = 0.002$) were observed during the 2006–2019 period (Figure 1). The significant increase in mortality was found for pancreatic cancer only (y = −98.5 + 0.05, $p = 0.005$). An insignificant decrease ($p > 0.05$) in mortality from cancer of colon and rectum/anus was observed.



The mortality rates of three digestive cancers (esophagus, stomach and liver) were positively correlated with consumption of milk (r = +0.718, +0.891 and +0.661, respectively), and negatively correlated with consumption of yoghurt (r = −0.556, −0.696 and −0.687, respectively) and consumption of other dairy (r = −0.600, −0.682 and −0.693, respectively) (Table 1). On the other hand, the mortality of pancreatic cancer was negatively

correlated with consumption of milk (r = −0.638), and positively correlated with consumption of yoghurt (r = +0.710) and consumption of other dairy (r = +0.693). In contrast, per capita consumption of none of the observed dairy products was correlated with colon and rectal / anus cancer mortality rates. Also, cheese consumption was not associated with mortality from any of the digestive cancers.

Table 1. Pearson's correlation coefficients (r) for *per capita* dairy consumption with mortality from digestive organs cancers (age-standardized mortality rates per 100 000 persons, using direct method, by Segi's World Standard Population) in Serbia, 2006–2019.

	Dairy Products (Unit)			
	Milk (L)	**Yoghurt (L)**	**Cheese (kg)**	**Other (L)**
Localization of cancers				
Esophagus	+0.718 **	−0.556 *	+0.172	−0.600 *
Stomach	+0.891 **	−0.696 **	+0.376	−0.682 **
Colon	+0.213	−0.114	−0.017	−0.085
Rectum/Anus	+0.414	−0.106	+0.028	−0.087
Liver	+0.661 *	−0.687 **	+0.062	−0.693 **
Pancreas	−0.638 *	+0.710 **	−0.108	+0.693 **

* $0.01 < p < 0.05$; ** $p < 0.01$.

In males, milk consumption was significantly positively related with cancer mortality rates from esophagus, stomach and rectum/anus ($p < 0.05$) (Table 2). Additionally, cheese consumption showed a significant negative association with cancer mortality rates from cancer of rectum/anus in males ($p = 0.019$). In females, consumption of milk showed significant positive association with mortality from stomach and rectum/anus cancer ($p = 0.002$ and 0.041, respectively). In both sexes, mortality from three localizations of digestive cancers (colon, liver and pancreas) was not associated with consumption of any dairy products.

Table 2. Association of the consumption of dairy products with mortality from digestive organs cancers, in Serbia, by sexes, 2006–2019; multivariate linear regression analysis.

	Males				**Females**			
Mortality	**Dairy items**	**β**	**95% CI**	***p* Value**	**Items**	**β**	**95% CI**	***p* Value**
Cancer								
Esophagus								
	Milk	+0.69	(0.01 to 0.13)	0.030				
Stomach								
	Milk	+0.18	(0.05 to 0.30)	0.013	Milk	+0.10	(0.05 to 0.16)	0.002
Colon								
Rectum/Anus								
	Milk	+0.13	(0.06 to 0.20)	0.003	Milk	+0.06	(0.01 to 0.13)	0.041
	Yoghurt	+0.31	(0.07 to 0.55)	0.017				
	Cheese	−0.74	(−1.13 to −0.15)	0.019				
Liver								

Pancreas			

Abbreviations: β, unstandardized coefficient; 95%CI, Confidence Interval; *p*—probability value according to multivariate linear regression analysis.

4. Discussion

One of the main findings in this study was the significant increase of mortality from pancreatic cancer, and significant decreased trends of mortality from cancer of esophagus, stomach and liver within the observed period in Serbia. Dairy products were strongly correlated with several types of digestive cancers, particularly milk consumption was linked with mortality from cancer of the esophagus, stomach and rectum/anus.

Observational studies have reported that migrants tended to reach similar incidence levels for colorectal cancer that those of natives in the host country: an estimated 60% drop of all cases could be due to modified eating habits [10], whereby estimated that milk consumption probably has a protective role in colorectal cancer occurrence.

A recent systematic review conducted to explain the association between dairy products and colorectal cancer risk in Middle Eastern and North African countries showed for dairy products overall that no significant association was found [11]. In one meta-analysis, dairy product consumption was associated with a non-significantly increased risk of gastric cancer [12]. In a population-based study in China, high milk consumption was associated with a higher risk of esophagus cancer mortality, while no significant association of high consumption with liver cancer, stomach cancer, or colorectal and anal cancer was found [13].

Consistent with others [8,9,14], our results showed significant differences in correlation between per capita consumption of dairy products for mortality rates of cancers among males and females. Overall, these findings do not support the hypothesis that consumption of dairy products is associated with pancreatic cancer risk. Besides, substantial differences according to sexes could be attributed to different exposure to lifestyle-related risk factors such as smoking habits, obesity and diabetes.

This ecological study has some limitations. In addition to the well-known shortcomings of ecological studies, a limitation of this study was the relatively short period studied. Besides well-known `ecological fallacy`, there were lack of control of confounding, some of collinearity and correlation that may not be linear.

5. Conclusions

Consumption of dairy is of potential importance for mortality of digestive cancers in Serbia. Further epidemiological analytical studies are needed to investigate a possible causative association.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of the Faculty of Medical Sciences, University of Kragujevac (Ref. No.: 01-14321, November 13, 2017), entitled "Epidemiology of the most common health disorders".

Informed Consent Statement: Not applicable. No patient approvals were sought nor required for this study. Namely, as our model-based analysis used aggregated data, patients were not involved in the research.

Data Availability Statement: Data is contained within the article.

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Conflicts of Interest: The authors declare no conflict of interest.

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