PUBLIC HEALTH

ASSESSMENT OF DISEASE BURDEN CAUSED BY BIOLOGICAL AGENTS ASSOCIATED WITH UNSAFE FOOD IN THE REPUBLIC OF NORTH MACEDONIA

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Key words: burden, biological agents, unsafe food, YLD, DALY

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Abstract

Diseases associated with unsafe food are common and cause significant public health and socioeconomic impact globally. The aim of the paper is to determine the burden of infections caused by biological agents at the national level and to determine the public health and economic impact. Material and methods: data from the national database of infectious diseases for 2019 were used, incidence, YLL, YLD, DALY and economic losses were determined. Results: In 2019, 7682 patients with diseases caused by biological agents were registered, of which 3755 or 48.9% were male patients and 3927 or 51.10 % were female patients. The most represented age group are people aged 6-15 (211 patients). The highest number of cases were registered in Skopje with 312 cases (32.8%). DALY is 1417,328 or 68.25 DALY per 100 000 population. The economic burden is 472 751 172 denars or 7 687 011 €. Conclusion: A better understanding of the true burden of foodborne disease is important for food safety policy making and decision making

ЈАВНО ЗДРАВЈЕ

ПРОЦЕНКА НА ОПТОВАРУВАЊЕ СО БОЛЕСТИ ПРЕДИЗВИКАНИ ОД БИОЛОШКИ АГЕНСИ ПОВРЗАНИ СО НЕБЕЗБЕДНА ХРАНА ВО РЕПУБЛИКА СЕВЕРНА МАКЕДОНИЈА

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Цитирање: Костова А, Ристовска Г, Гудева Никовска Д. Проценка на оптоварување со болести предизвикани од биолошки агенси поврзани со небезбедна храна во Република Северна Македонија Арх Ј Здравје 2025;17 (1) 26-39.

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Клучни зборови: оптовареност,биолошки агенси, небезбедна храна,YLD, DALY

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Печатарски права: ©2025. Анета Костова, Гордана Ристовска, Данче Гудева Никовска. Оваа статија е со отворен пристап дистрибуирана под условите на нелокализирана лиценца, која овозможува неограничена употреба, дистрибуција и репродукција на било кој медиум, доколку се цитираа торигиналниот(ите) автор(и) и изворот.

Конкурентски интереси: Авторот изјавува дека нема конкурентски интереси.

Извадок

Болестите поврзани со небезбедна храна, се чести и предизвикуваат значително јавно здравствено и социоекономско влијание на глобално ниво. Цел на трудот е да се одреди оптоварувањето со болести предизвикани со биолошки агенси на национално ниво и да се утврди јавно здравственото и економското влијание. Материјал и методи: користени се податоци од националната датабаза на заразни болести за 2019 година, одредена е инциденца, YLL, YLD, DALY и економските губитоци. Резултати: Во 2019 година регистрирани се 7682 заболени лица од болести предизвикани од биолошки агенси, од кои 3755 или 48,9% пациенти од машки пол и 3927 или 51,1% пациенти од женски пол. Најзастапена возрасна група се лицата од 6-15 години (211 пациенти). Највисок број на случаи се регистрирани во Скопје со 312 случаи (32,8%). DALY изнесува 1417,328 или 68,25 DALY на 100 000 население. Економското оптоварување изнесува 472 751 172 денари или 7 687 011 €. Заклучок: Подоброто разбирање на вистинската оптовареност на болестите што се пренесуваат преку храна е важно за креирање на политиката за безбедност на храна и донесување одлуки.

Introduction

The concept of burden of disease assessment was developed in the 1990s by the Harvard School of Public Health, the World Bank and the WHO to describe death and loss of health due to disease, injury and risk factors for all regions of the world[1] While the burden of disease can be expressed using a variety of indicators, such as incidence, mortality, societal costs, and aggregate measures of population health, this study introduced a new metric, Disability Adjusted Life Years (DALY), which combines information on morbidity and mortality caused by diseases. The DALY is now the most widely used public health metric for disease burden studies and the key measure in the Global Burden of Disease studies[2]

The first estimates of the burden of disease associated with unsafe food, measured in Disability Adjusted Life Years (DALYs), were published in 2000, focusing on a single foodborne pathogen in the Netherlands[3]. In 2015, the World Health Organization (WHO) released the first global DALY estimate for the burden of foodborne diseases. Several countries, including the Netherlands, Japan, Denmark, Belgium, and the United States[4], have since conducted studies on foodborne disease burden, primarily targeting microbial agents.

Low-income countries are beginning to address knowledge gaps in this area. For instance, Rwanda[5] has estimated the incidence of foodborne diseases using syndromic surveillance data, and the Caribbean Burden of Disease Study[6] has assessed the prevalence and incidence of acute gastroenteritis and specific foodborne pathogens across nine countries. These initiatives represent initial steps towards comprehensive national disease burden studies.

The initial step in each national study was to identify food supply hazards relevant to the pilot country. Lists of hazards and associated diseases that were compiled, with each country adding predicted hazards significant from their perspective.[7] Available information on the incidence of diseases associated with these hazards and the prevalence of the hazards in the food supply was then collected. These data were summarized, and the disease burden was attributed to specific foods based on the available data.[8]

The Global Burden of Disease Study 2010, conducted by the Institute for Health Metrics and Evaluation in Seattle USA, encompasses a broad spectrum of diseases and injuries, providing country-specific estimates.[9] National studies on food-related diseases, promoted by WHO and Foodborne Disease Burden Epidemiology Reference Group (FERG), incorporate situation analysis that considers the national context, including the existing national food control system.[10]

National studies of the burden of food-related disease, particularly in developing countries, now have the opportunity to address data gaps and assign etiology and attribution to the incidence of food-related disease, by leveraging data from the WHO initiative and local sources. [11] Information on the burden of disease associated with unsafe food should be a core component to a systematic approach to food safety, as advocated by the Codex risk management framework.[12] Such an approach can enhance public health and facilitate trade.

Estimating the burden of disease as-

sociated with unsafe food is challenging because few diseases can be definitively linked to food, with connections often identified only during outbreak situations.[13] Although not all acute gastrointestinal illnesses are foodborne and foodborne illnesses do not always result in acute gastroenteritis, food remains a significant vector for pathogens that cause acute gastroenteritis.[14]

Diseases associated with unsafe food are prevalent and have significant public health and socioeconomic impact globally.[15] The World Health Organization (WHO) estimated that, in 2010, 22 foodborne enteric pathogens have caused two billion illnesses, over one million deaths, and 78.7 million DALYs. While intestinal disease often manifests as a self-limiting AGI, presenting as diarrhea or vomiting, they can lead to severe illness and even death[16].

The aim of this study is to quantify the national burden of infections caused by biological agents related to unsafe food and to assess their public health and economic impacts. Sub-objectives of the paper are:

- To determine the incidence and morbidity of infections caused by biological agents. related to unsafe food during 2019;
- To quantify the burden of these infections using DALY indicator
- To assess the economic impact of infections caused by biological agents related to unsafe food.

Materials and methods

Data from the national database for infectious diseases, maintained by the Institute of Public Health of the Republic of North Macedonia was utilized for the year 2019. Family physicians are mandated to complete a notification form for each occurrence of an infectious disease among patients. These forms are submitted to the Centers for Public Health, which then forward the information to the Public Health Institute of North Macedonia.

This study employs the DALY measure, which integrates data on morbidity, mortality and disability caused by diseases. DALY is a more comprehensive metric than incidence or prevalence rate; it is now the most widely used public health metric for disease burden studies, serving as the key measure in the Global Burden of Disease (GBD) Study.

DALY quantifies the health gap by measuring the years of healthy life lost due to disease or risk factors. It is calculated by summing the years of life lost due to premature mortality (YLL) and the years lived with disability (YLD), adjusted for the severity of the disability:

DALY=YLL+YLD

YLL is the product of the number of deaths (M) and the average remaining life expectancy (RLE) at the time of death:

YLL=M x RLE

The 2010 GBD study introduced a prevalence based approach to calculating burden of disease. This method assesses the current burden of disease as a consequence of past events, evaluating the health status of a population at a specific point in time and attributing prevalent diseases to initial events that occurred previously. While the definition of YLL remains consistent with the incidence-based approach, YLD is defined as the prod-

uct of the number of prevalent cases (P) and the disability weight (DW). The disability weight reflects the reduction in health-related quality of life on a scale from 0 (no effect on full health) to 1 (death).

YLDprev=P x DW

To estimate YLL, the use of a standard life table is recommended, to reflect the ideal life expectancy, based on the lowest possible mortality given the currently available data. Various standard life tables have been developed for the WHO Global Health Assessment (GHA) and GBD studies by the Institute for Health Metrics and Evaluation (IHME).

However, for this study, we will utilize the life table specific to the Republic of North Macedonia. The weight of each health outcome is represented by disability weights (DW), which range from 0 to 1, where 0 represents full health and 1 represents death. DW can be interpreted as a proportional decrease in good health due to an adverse health condition.

The study used WHO methodology.11

Given the difficulty of making detailed estimates of the value of YLL or YLD, a frequently used shortcut is to use a country's per capita gross domestic product (GDP) as a measure of lost productivity. For every year lost to illness, disability or premature death, the country loses the economic output associated with that year. Foodborne disease is therefore represented as a drain on the country's productivity. The calculation is represented by the following formula:

$VPi = Bi \times Yi$

where VPi is the value of productivity losses associated with foodborne diseases in country i; Bi is the total DALY burden of foodborne diseases in country i; and Yi is GDP per capita for country i. We will express this value in local currency (Denars) or in Euros to allow comparison between countries.

Chi-square one- or two-sample test were used to compare specific features between two groups. Cramer'V was used to determine the association between two nominal variables.

Results

In 2019, 7682 cases of diseases related to unsafe food were registered. 12 foodborne diseses were reported to IPH, in the database of infectious diseases, representing alimentary diseases.

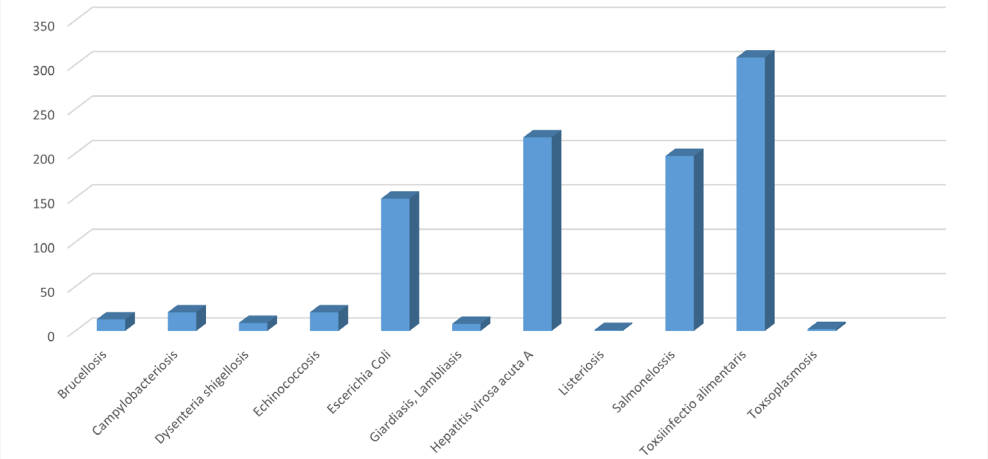


Chart 1: Total number of diseases related to unsafe food

From the total number of food-borne diseases, the largest number of diseases are Enterocolitis with 6735 cases, then Bacterial alimentary infections and intoxications with 308 cases, Viral Hepatitis A with 218 cases, Salmonellosis with 197 cases, Echinococcosis with 21 cases Campylobacteriosis with 21 cases, Brucellosis with 13 cases, Shigellosis with 9 cases and Giardiasis with 8 cases. The lowest number of foodborne diseases is Listeriosis with 1 case, followed by Toxoplasmosis with 2 cases. The structure of diseases related to unsafe food is shown in Chart 1.

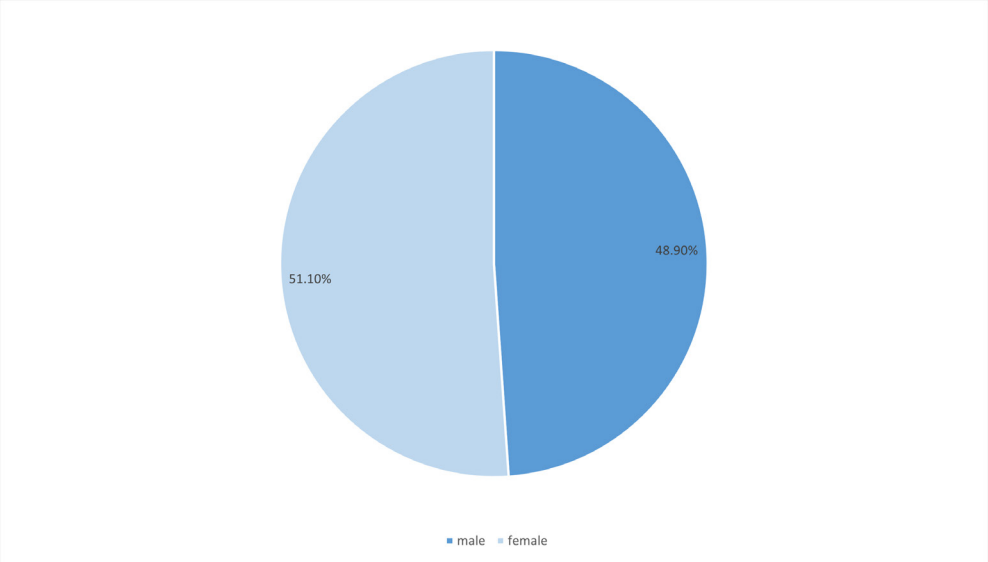


Chart 2: Structure by gender of patients with diseases related to unsafe food

The analysis included 7682 patients suffering from diseases related to unsafe food, of which 3755 or 48.90% were male patients and 3927 or 51.10% were female patients (Graph 2)

The gender analysis did not find statistically significant difference between male and female patients (Chi-square:3.336; df=1; p=0.068)

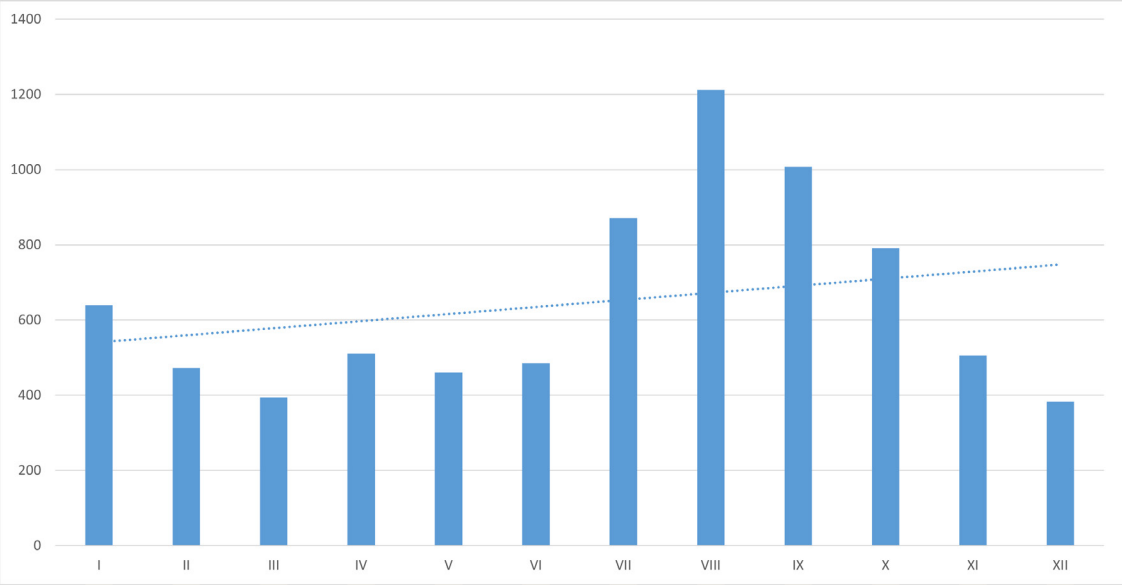


Chart 3: Seasonal occurrence of foodborne diseses by month

In terms of seasonal changes, the largest number of diseases occurred in the month of August with 1212 cases, in the month of September with 1007 cases, in the month of July with 871 cases. The lowest number of cases occurred in the month of December with 383 cases, and then in the month of March with 394 cases. The seasonal occurrence of BNH is shown in Chart 3. The graphic display indicates an increasing trend of diseases by month for 2019.

Data on Enterocolitis was not analyzed, as this diagnosis was not entered into the database of the Public Health Institute.

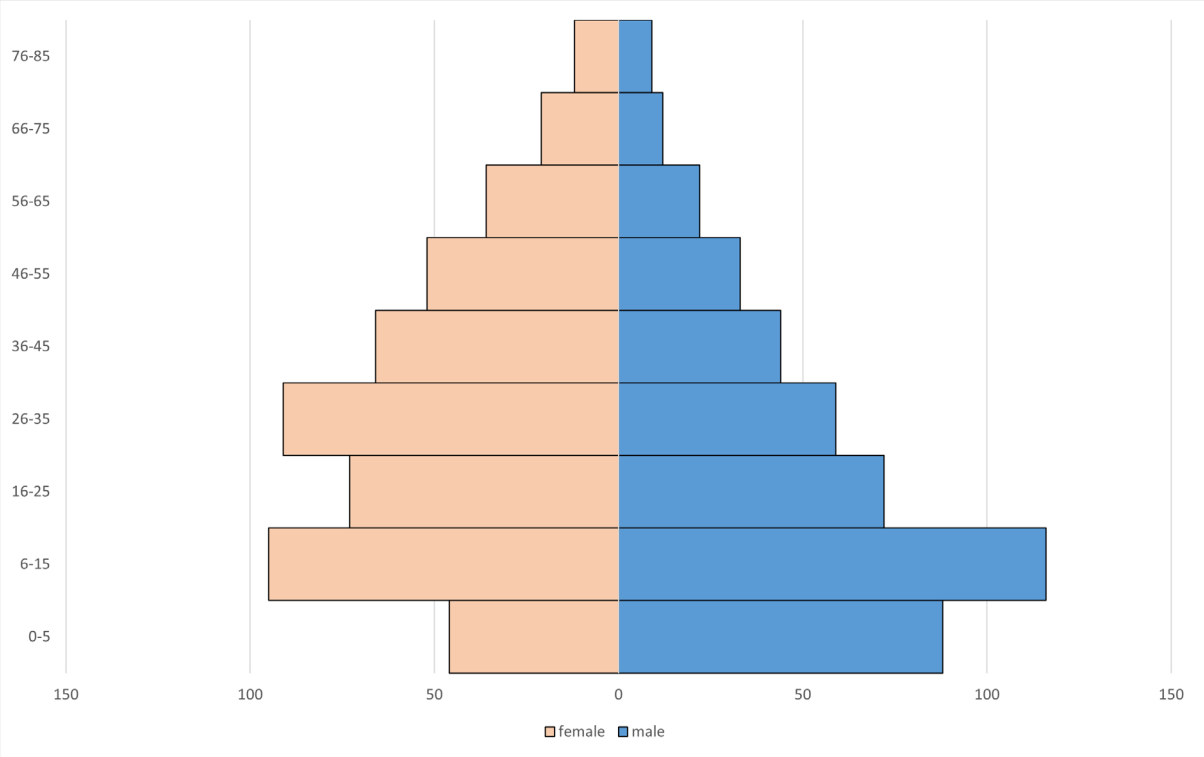


Chart 4: Presentation of the age pyramid for foodborne disesases

In terms of age, the most represented group for female patients is 6-15 years old (95 patients), then 26-35 years old (91 patients) and 16-25 years old (73 patients). The least represented age group for female patients is 76-85 years (12 patients), followed by the age group 66-75 years (21 patients). Regarding male patients, the most represented age group is from 6-15 years (116 patients), followed by the age group from 0-5 years (88 patients). The least represented age group for male patients is 76-85 years (9 patients), followed by the age group 66-75 years (12 patients). The structure by age groups of patients is shown in Chart 4.

In 2019, the highest number of cases with foodborne diseases were registered in Skopje with 312 cases (32.8%), followed by Bitola with 122 cases (12.8%) and Kumanovo with 112 cases (11.8%). In the same period, the lowest number of cases were registered in Debar and Pehčevo with only one case (0.1%). The graphic presentation of cases of diseases related to unsafe food by municipality is presented in Graph 5.

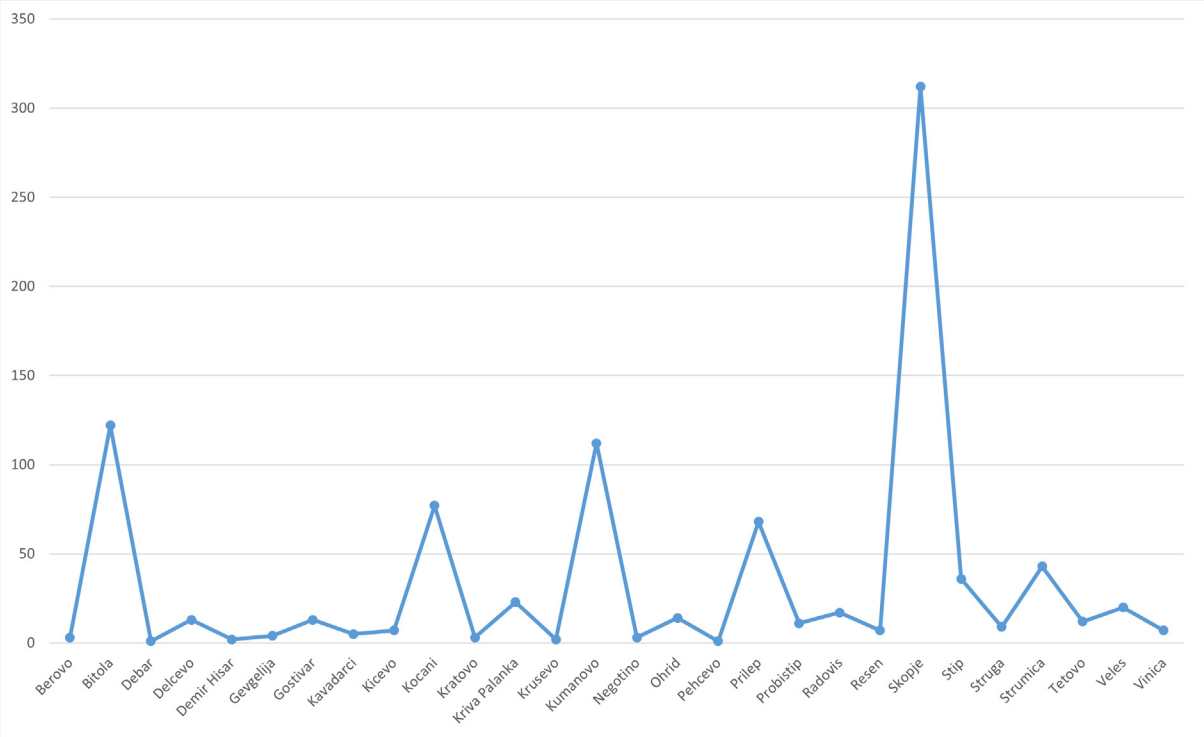


Chart 5: Presentation of foodborne diseases cases by municipalities

Within the analysis of the structure of patients in relation to employment status, it was observed that 283 (29.8%) patients are employed, 231 (24.3%) are students, 162 (17.0%) are unemployed, 151 are children. (15.9%), pensioners are 58 (6.1%), housewives are 38 (4.0%), primary and secondary school students are 16 (1.7%) and refugees are 10 (1.1%).

The difference between persons with foodborne diseases in terms of employment status shows statistically significant difference between groups (Chi-square:632.952; df=7; p<0.001)

Table 1: Hospitalization for foodborne diseases according to gender

		hospitalization		Total
		yes	no	
Gender	male	144 (15.2%)	311 (32.8%)	457 (48.0%)
	female	223 (23.5%)	269 (28.4%)	492 (52.0%)
Total		367 (38.8%)	580 (61.2%)	947 (100%)

Regarding hospitalization, the analysis showed that male patients were hospitalized in 144 (15.2%) cases, while female patients were hospitalized in 223 (23.5%) cases. Male patients were not hospitalized in 311 (32.8%) cases, while female patients were not hospitalized in 269 (28.4%) cases (Table 1)

The analysis showed statistically significant difference between patient gender and hospitalization (Chi-square: 18.630; df=1; p<0.001).

The analysis showed high association between patient gender and hospitalization (Cramer's V:0.714; p<0.001).

Table 2: Hospitalization for foodborne diseases by employment status

		Hospitalization		Total
		Yes	no	
Work status	Child	47 (5.0%)	104 (11.0%)	151 (15.9%)
	Pupil	66 (7.0%)	164 (17.3%)	230 (24.3%)
	Student	8 (0.8%)	8 (0.8%)	16 (1.7%)
	Worker	120 (12.7%)	162 (17.1%)	282 (29.8%)
	Unemployed	68 (17.2%)	94 (9.9%)	162 (17.1%)
	Housewife	20 (2.1%)	18 (1.9%)	38 (4.0%)
	Pensioner	28 (3.0%)	30 (3.2%)	58 (6.1%)
	Refugee	10 (1.1%)	0	10 (1.1%)
Total		367 (38.8%)	580 (61.2%)	947 (100%)

Regarding hospitalization by employment status, the analysis showed that the largest number of hospitalized patients were employed 120 (12.7%), unemployed 68 (17.2%), students 66 (7.0%) The smallest number of hospitalized patients were students in primary and secondary school 8 (0.8%). While students were not hospitalized in 164 (17.3%) cases, workers were not hospitalized in 162 (17.1%) cases and unemployed patients were not hospitalized in 94 (9.9%) cases. (Table 2).

The analysis by groups showed statistically significant difference between the structure of patients by employment status and hospitalization (Chi-square: 37.884; df=7; p<0.001). The analysis showed moderate association between the structure of patients by employment status and hospitalization (Cramer's V: 0.201; p<0.001).

Data analysis showed statistically significant difference between laboratory-confirmed diagnosis and hospitalization among patients with food-related illnesses. (Chi-square:16.038; df=1; p<0.001). The analysis showed low association between laboratory-determined diagnosis and hospitalization (Cramer's V: 0.130; p<0.001).

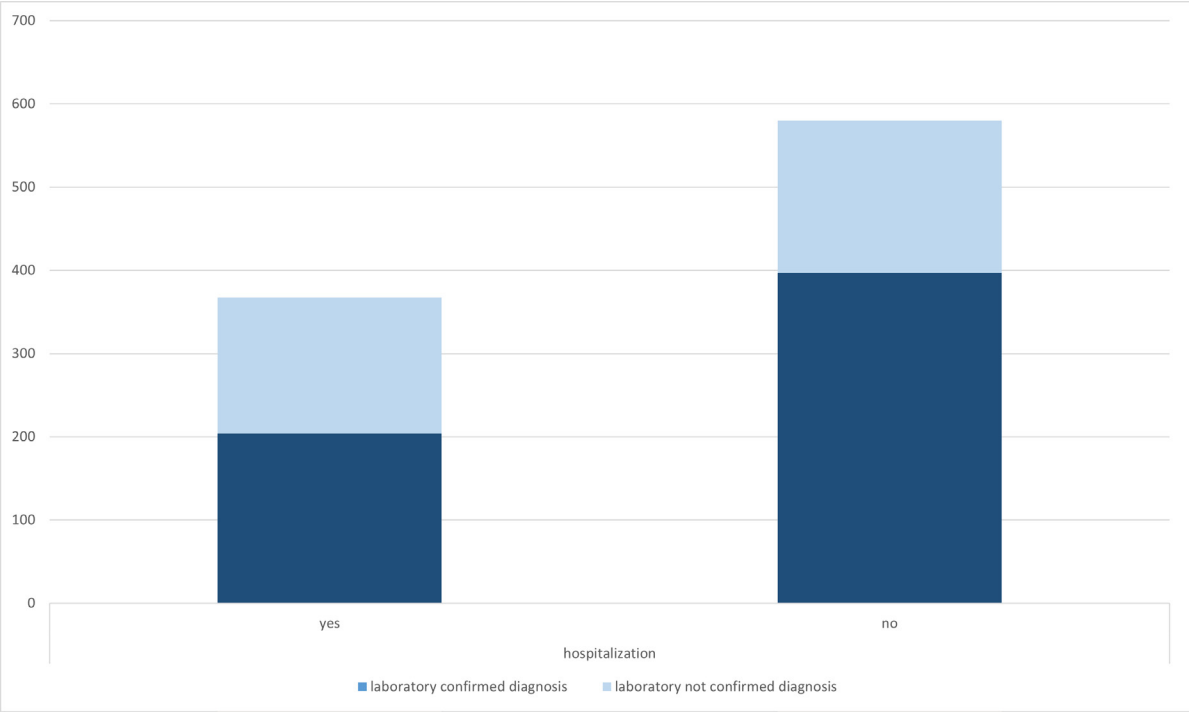


Chart 6: Presentation of patients with total diseases related to unsafe food in relation to laboratory-confirmed diagnosis and hospitalization

Data analysis showed statistically significant difference between clinically confirmed diagnosis and hospitalization among patients with food-related illnesses (Chi-square: 21.110; df=1; $p<0.001$). The analysis showed low association between clinically confirmed diagnosis and hospitalization (Cramer's V: 0.149; $p<0.001$).

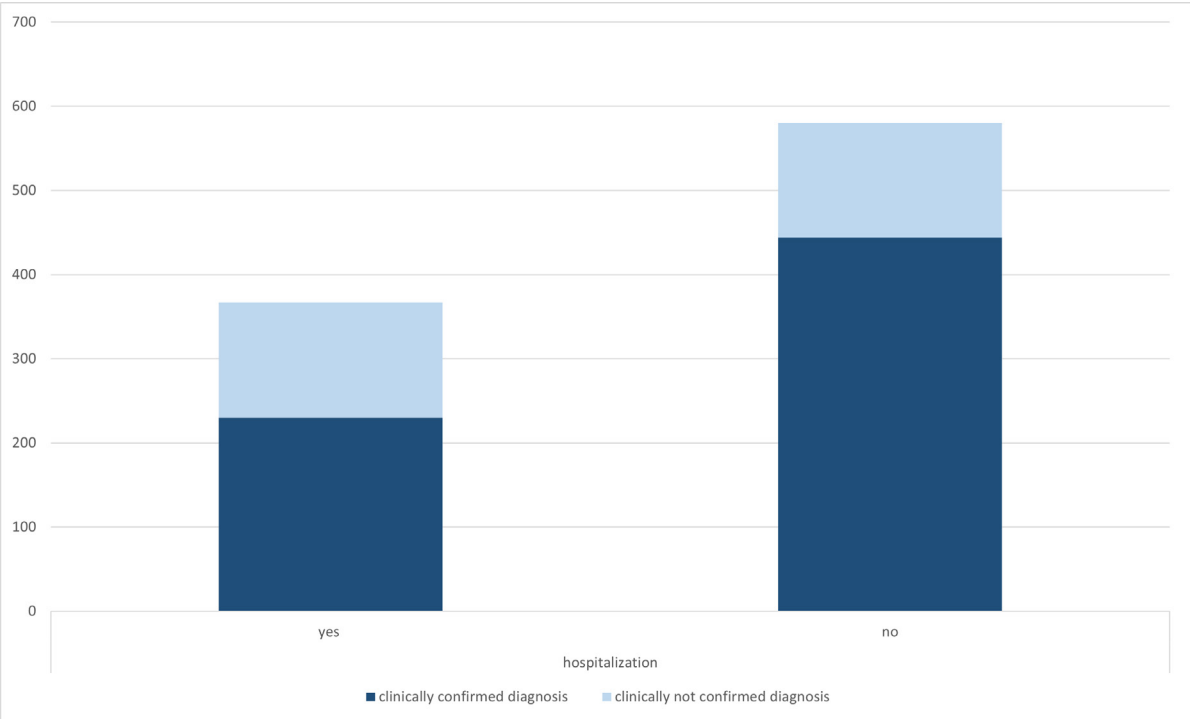


Chart 7: Presentation of patients with foodborne diseases related to unsafe food in relation to clinically confirmed diagnosis and hospitalization

Pathogen	Number of cases	Morbidity Per 100,000 population	YLL	YLD	DALY	DALYs per 100 000 population
Bacterial alimentary infections and intoxications	308	14,83	0	58	58	2,8
Brucellosis	13	0,63	0	1,404	1,404	0,068
Virus Hepatitis A	218	10,5	0	23,54	23,54	1,133
Enterocolitis	6735	324,38	0	1266,18	1266,18	60,97
Echinococcosis	21	1,01	0	4,032	4,032	0,194
Escherichia coli infections	149	7,18	0	11,03	11,03	0,53
Campylobacteriosis	21	1,01	0	2,12	2,12	0,102
Listeriosis	1	0,05	29,3	0,210	29,51	1,42
Salmonellosis	197	9,49	0	19,9	19,9	0,96
Toxoplasmosis	2	0,096	0	0,11	0,11	0,005
Giardiasis	8	0,39	0	0,592	0,592	0,0285
Shigellosis	9	0,433	0	0,91	0,91	0,0438
Total	**7682**	**370,08**	**29,3**	**1388,03**	**1417,328**	**68,25**

DALYs and economic burden of foodborne diseases

The morbidity rate of total diseases related to unsafe food is 370.0 per 100 000 population

Mb = (O/S) x K = (7682/2076255) x 100 000 = 370.0 (5)

The sex-specific morbidity rate is 378.8 per 100,000 population for women and 361.1 per 100,000 population for men.

Mbfemales = (3927 / 1036736) x 100 000 = 378.8

Mbmales = (3755 / 1039958) x 100,000 = 361.1

The incidence rate is 3.7 per 1000 population

Incidence rate = (7682/2076255) x 1000 = 3.7

DALY = YLL + YLD

ΣDALY = 58 + 1.404 + 23.54 + 1266.18 + 4.032 + 11.03 + 2.12 + 29.51 + 19.9 + 0.11 + 0.592

+ 0.91 =1417.328

DALY is 1417.328 or 68.25 DALY per 100 000 population

DALYfemales = 724.25

DALYmales = 693.07

The value of productivity losses is 472 751 172 denars or 7 687 011 € or 8 601 106 USD

DALY x GDP = 1417.328 x 333,551 denars = 472,751,172 denars

The gross domestic product in the Republic of North Macedonia for 2019 is 689 425 000 000 denars, of which the agriculture, forestry and fishing sector (gross domestic product according to the production method) is 55 477 000 000 denars.

The value of productivity losses is 0.852% of the assets of the agriculture, forestry and fisheries sector.

Discussion

Our research reveals that unsafe food-related diseases impose a significant global health burden, to-

taling 1,417.328 Disability-Adjusted Life Years (DALYs), equivalent to 68.25 DALYs per 100,000 population. This figure surpasses the European region's burden, where EUR A reports 41 DALYs, EUR B (including the Republic of North Macedonia) 52 DALYs, and EUR C 49 DALYs per 100,000 population[17].

Globally, a 2010 study on unsafe food-related illnesses estimated 600,652,361 cases, resulting in 418,608 deaths. These diseases accounted for 32,841,428 DALYs, including 5,589,028 Years Lived with Disability (YLDs) and 27,201,701 Years of Life Lost (YLLs)17. Regionally, the burden varies significantly:

- Eastern Mediterranean: EMR B at 362 DALYs and EMR D at 571 DALYs per 100,000 population.
- North America: AMR A at 35 DALYs, AMR B at 140 DALYs, and AMR D at 315 DALYs per 100,000 population.
- Western Pacific: WPR A at 36 DALYs and WPR B at 293 DALYs per 100,000 population.
- South-East Asia: SEAR B at 685 DALYs and SEAR D at 711 DALYs per 100,000 population.
- These findings underscore the urgent need for targeted interventions to address the disproportionate impact of unsafe food across regions.

A 2010 study on the global burden of unsafe food-related diseases found that diarrheal disease agents caused 548,595,679 cases worldwide, resulting in 230,111 deaths. These agents contributed to 17,659,226 Disability-Adjusted Life Years (DALYs), including 839,463 Years Lived with Disability (YLDs) and 16,821,418 Years of Life Lost (YLLs).

Regionally, the burden of diarrheal diseases varied significantly:

- South-East Asia: SEAR B at 330 DALYs and SEAR D at 380 DALYs per 100,000 population.
- Eastern Mediterranean: EMR B at 277 DALYs and EMR D at 393 DALYs per 100,000 population.
- North America: AMR A at 23 DALYs, AMR B at 60 DALYs, and AMR D at 72 DALYs per 100,000 population.
- Western Pacific: WPR A at 23 DALYs and WPR B at 41 DALYs per 100,000 population.
- Europe: EUR A at 28 DALYs, EUR B (including the Republic of North Macedonia) at 25 DALYs, and EUR C at 24 DALYs per 100,000 population.

The study also estimated that 31 hazardous agents in unsafe food caused a total of 33 million DALYs in 2010, comparable to major infectious diseases like HIV/AIDS (92 million DALYs), malaria (55 million DALYs), and tuberculosis (44 million DALYs). This burden is also similar to other risk factors, including poor diet (254 million DALYs), inadequate water and sanitation (211 million DALYs), and air pollution (76 million DALYs)[18]. These findings highlight the critical public health challenge posed by unsafe food and the need for robust global interventions.

Our study estimates productivity losses from unsafe food-related diseases at 472,751,172 MKD (7,687,011

EUR or 8,601,106 USD). Comparative studies highlight the global economic burden of foodborne illnesses:

- New Zealand (2010): Total costs reached 161.9 million NZD, including 16.4 million NZD in government costs, 12.3 million NZD in industry costs, and 133.2 million NZD in disease-related costs (treatment, lost output, and lifestyle impacts)19.
- Australia (2019): Foodborne illnesses cost 2.44 billion AUD annually (90% uncertainty interval: 1.65–3.68 billion), with Campylobacter, non-typhoidal Salmonella, Shiga toxin-producing E. coli, and norovirus as leading contributors[20].
- Denmark (2019): Seven food-related diseases generated a burden of 434 million EUR[21].
- United States (2015): Foodborne pathogens imposed a 15.5 billion USD economic burden annually, with five pathogens accounting for 90% of the costs[22].

These findings underscore the substantial economic impact of unsafe food across diverse economies, highlighting the need for targeted prevention and control measures.

- The first-ever estimates of foodborne diseases in the Republic of North Macedonia reveal a significant public health burden. The ranking of diseases, deaths, and Disability-Adjusted Life Years (DALYs) per hazard varies widely, with diarrheal disease agents identified as the primary contributors to illness. Notably, hazards causing the most cases do not always rank highest in deaths or DALYs. This discrepancy indicates that high-case-count diseases draw greater public health attention, while less frequent but severe diseases impose a substantial, often underrecognized burden. Factors such as symptom severity, duration, case fatality ratio, and age at death reshape the understanding of foodborne illnesses and highlight the need to prioritize both prevalent and severe hazards in public health strategies.[18]

Conclusion

A comprehensive understanding of the true burden of foodborne disease is crucial for developing evidence-based food safety policies and making informed decisions. Disability Adjusted Life Years (DALY) estimates provide a clear illustration of the impact of foodborne diseases in the European Region, enabling comparisons across different diseases and their effects on the population. This approach is essential for prioritizing food safety management efforts and formulating targeted policies to address foodborne diseases.

The Foodborne Disease Burden Epidemiology Reference Group (FERG) estimates offer a valuable resource, encouraging and guiding countries to conduct their own studies on the burden of foodborne disease. The World Health Organization (WHO) has provided tools to facilitate these studies, allowing countries to analyze the disease burden associated with food contamination and to describe the epidemiology of foodborne illness. These studies promote the

use of evidence-based information in food safety policy and decision-making, including setting priorities, enhancing risk communication, and raising food safety awareness. Ultimately, this approach helps prevent foodborne illness at both national and regional levels, improving public health and economic outcomes.

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