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The Moldovan Association for Biosafety and Biosecurity (MDBBA) is a scientific and practical, instructive and educational, non-governmental, apolitical and non-profit professional organization, founded in 2017.

The main objective of the association is the development of good practices and culture in the field of biosafety and biosecurity and the promotion of knowledge within professional and research-innovation groups.

BIOSAFETY includes security principles, technologies and rules to be followed to prevent unintended exposure to pathogens and toxins or their accidental release/ leakage.

"Protection of personnel, population from unintended exposure to pathogens/ biohazardous material".

BIOSECURITY includes a wide spectrum of measures (biosecurity policies, regulatory regime, scientific and technical measures) applied in an organized framework, necessary to minimize risks (prevention of actions, terrorist attacks by the intentional release of pathogens or toxins as well as loss, their theft or misuse).

"Protection and prevention of theft, intentional misuse of pathologies/biohazardous material".

RISK MANAGEMENT is a decision-making process in which the results of risk assessment (the process of estimating workplace hazards) are integrated with economic, technical, social and political principles to generate strategies for risk reduction.

One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems.

It recognizes that the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent.

While health, food, water, energy and environment are all wider topics with sector-specific concerns, the collaboration across sectors and disciplines contributes to protect health, address health challenges such as the emergence of infectious diseases, antimicrobial resistance, and food safety and promote the health and integrity of our ecosystems.

By linking humans, animals and the environment, One Health can help to address the full spectrum of disease control – from prevention to detection, preparedness, response and management – and contribute to global health security.

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Enhancing BWC Implementation in Moldova

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The Biological Weapons Convention (BWC) celebrates its 50th anniversary this year. Building on the foundations of the 1925 Geneva Protocol, the Convention has established a strong and comprehensive norm against an entire category of Weapons of Mass Destruction.

Recognizing the evolving risks posed by rapid scientific advancements and the dual-use nature of life sciences, the Republic of Moldova, a State Party to the Convention since 2005, recently appointed its National Agency for Public Health as its BWC National Contact Point to strengthen national implementation and collaboration.

The BWC Implementation Support Unit looks forward to working closely with the National Agency for Public Health in the Republic of Moldova to further strengthen the national implementation of the Convention and congratulates the Moldavian Biosafety and Biosecurity Association on its publication "One Health & Risk Management" in support of these efforts.

Dr. Alex Lampalzer

RESEARCH ARTICLES – ARTICLES DE RECHERCHE

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EXPLORING THE RELATIONSHIP BETWEEN DIETARY PATTERNS AND THE RS2241766 POLYMORPHISM IN THE ADIPONECTIN GENE IN CORONARY ARTERY DISEASE: A GENE-DIET INTERACTION STUDY

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ABSTRACT:

Introduction The coronary artery disease remains a major health issue worldwide, especially in low- and middle-income countries where genetic predispositions significantly contribute to its prevalence.

Materials and methods This study, conducted at Chettinad Hospital and Research Institute, Kelambakkam, India, from January to April 2024, investigates the relationship between dietary patterns, genetic variations in Adiponectin, and coronary artery disease risk. Genetic analysis of the adiponectin (45T/G) polymorphism was performed using the Tetra-primer Amplification Refractory Mutation System Polymerase Chain Reaction method.

Rezults The results revealed notable links between genetic variations, dietary behaviours, and health indicators coronary artery disease patients. Anthropometric and biochemical measurements showed that narrowed coronary arteries were associated with elevated BMI and waist circumference. Lifestyle and sleep patterns also differed significantly between the groups. Among coronary artery disease participants, 64% followed non-vegetarian diets, with higher consumption of red meat and fast food, negatively impacting lipid profiles. The rs2241766 GG genotype of the adiponectin gene was significantly associated with these dietary habits ($p<0.01$) and obesity (OR=5.1429, p=0.0084). Similarly, the GT genotype demonstrated a strong correlation with obesity (OR=22.15, $p < 0.050$).

Conclusions This study highlights the intricate connections between genetic predispositions, dietary choices, and coronary artery disease risk. The rs2241766 GG genotype emerged as a strong predictor of coronary artery disease susceptibility compared to the rs2231142 TT genotype, emphasizing the complex interplay of diet, genetics and obesity in coronary artery disease development.

Keywords Gene-Diet interaction, adiponectin Rs2241766, coronary artery disease, genotype, dietary pattern.

EXPLORAREA RELAȚIEI DINTRE MODELE DE DIETE ȘI POLIMORFISMUL RS2241766 ÎN GENA ADIPONECTINEI ÎN BOALA CORONARIANĂ: UN STUDIU DE INTERACȚIUNE GENĂ-DIETĂ

Introducere Boala coronariană rămâne a fi o problemă majoră de sănătate la nivel global, în special în țările cu venituri mici și medii, unde predispozițiile genetice contribuie în mod semnificativ la prevalența acesteia.

Materiale și metode Studiul a fost realizat la Chettinad Hospital and Research Institute, Kelambakkam, India, din ianuarie până în aprilie 2024, și a investigat relația dintre regimurile alimentare, variațiile genetice ale adiponectinei și riscul de boală coronariană. Analiza genetică a polimorfismului adiponectinei (45T/G) a fost efectuată utilizând metoda Tetra-primer Amplification Refractory Mutation System Polymerase Chain Reaction.

Rezultate Au fost evidențiate legături notabile între variațiile genetice, comportamentele alimentare și indicatorii de sănătate la pacienții cu boală coronariană. Măsurătorile antropometrice și biochimice au demonstrat că arterele coronare îngustate au fost asociate cu indicele de masă corporală și circumferința taliei crescute. Printre participanții cu boli coronariene, 64% au urmat diete non-vegetariene, cu un consum mai mare de carne roșie și fast-food, influențând negativ profilurile lipidice. Genotipul rs 2241766 GG al genei adiponectinei a fost asociat semnificativ cu aceste obiceiuri alimentare ($p<0,01$) și cu obezitatea (OR=5,1429, p=0,0084). În mod similar, genotipul GT a demonstrat o corelație puternică cu obezitatea (OR=22,15, $p <0,050$).

Concluzii Acest studiu relevă conexiunile polivalente dintre predispozițiile genetice, selectarea dietei și riscul de afecțiune coronariană. Genotipul rs2241766 GG s-a manifestat ca un predictor puternic al susceptibilității la boala coronariană în comparație cu genotipul rs2231142 TT, subliniind interacțiunea complexă a dietei, geneticii și a obezității în dezvoltarea bolii coronariene.

Cuvinte cheie Interacțiunea genă-dietă, adiponectina Rs 2241766, boala coronariană, genotip, tipar alimentar.

INTRODUCTION

Coronary artery disease (CAD) results from plaque build-up in coronary arteries, restricting blood flow to the heart. Although CAD mortality has declined since the 1960s, it remains a leading cause of death. Atherosclerosis, driven by preventable factors like hypertension and smoking, as well as non-modifiable risks like age and genetics, leads to endothelial dysfunction and plaque formation (1-5). Diet plays a crucial role in CAD risk, with plant-based diets (PBDs) reducing the risk by up to 29% by preventing endothelial damage, LDL oxidation, and macrophage activation (6). CAD has a heritability of 40-60%, with genetic variations (SNPs) linked to disease susceptibility. Genome-wide association studies (GWAS) have identified SNPs associated with CAD. Adiponectin, which regulates metabolism, correlates with CAD, obesity, and diabetes. Genetic factors, including polymorphisms in the adiponectin gene, interact with diet to influence health outcomes (7-15). This cross-sectional study in South India explored the relationship between dietary patterns and the rs2241766 SNP in the adiponectin gene, aiming to understand its association with CAD and improve health outcomes.

MATERIALS AND METHODS

STUDY DESIGN AND POPULATION

This cross-sectional study was conducted at Chettinad Hospital and Research Institute (Chennai) from January to March 2024. It included 50 participants: 25 with Coronary Artery Disease (CAD) and 25 healthy controls, aged 30-70 (mean age: 45.4 ±12.81). Participants were excluded if they had chronic conditions, were pregnant or lactating, or used alcohol or tobacco. The study was approved by the Institutional Ethics Committee.

QUESTIONNAIRE

A semi-structured Food Frequency Questionnaire (FFQ) with 12 food groups was used to gather demographic, lifestyle, and dietary data. It captured food consumption frequency ranging from “never” to “2 or more times a day”, ensuring cultural relevance and aligning with study objectives.

ANTHROPOMETRIC DETAILS

Height, weight, BMI (calculated as weight in kg/height in m^2), and waist-to-hip ratio (WHR) were measured using standard procedures.

BIOCHEMICAL ANALYSIS

Blood samples were collected to measure cholesterol levels (TC, TG, HDL-C, LDL, VLDL), fasting blood glucose (hexokinase method), HbA1c (HPLC method), and cardiac markers (Trop-I, BNP, CK-MB) using Siemens and Beckman Coulter analyzers.

DNA EXTRACTION AND GENOTYPING

DNA was extracted from peripheral blood leukocytes and analyzed for the ADIPOQ-RS2241766 SNP using Tetra-primer ARMS PCR. The PCR products were analyzed by agarose gel electrophoresis.

DIETARY CLASSIFICATION

Dietary patterns were classified into 10 food groups based on nutrient profiles, including categories such as red meat, seafood, fast food, and high-salt diets.

STATISTICAL ANALYSIS

Descriptive statistics summarized categorical variables, and continuous variables were expressed as mean ± standard deviation. An independent t-test was used to compare CAD and non-CAD groups. Pearson's correlation analyzed biochemical and food group relationships. Genotype distribution was assessed using Hardy-Weinberg equilibrium and Fisher's exact test. Odds ratios were calculated for genotype and dietary pattern associations. Statistical significance was set at $p < 0.05$, with analysis conducted using IBM SPSS version 29.0.

RESULTS

The table presents the mean and standard deviation (SD) values for various clinical and biochemical parameters, comparing overall (N=50), CAD group shows significantly higher glycaemic levels, lipid abnormalities, and elevated cardiac markers, indicating higher cardiovascular risk compared to non-CAD group.

Table 1. Characteristics of the Participants.

Parameters	N=50 Mean± SD	CAD group Mean ± SD	Non - CAD group Mean ± SD
AGE (yrs)	45.4 ±12.81	45.63 ±14.18	42.64 ±10.67
BMI kg/m2	23.3 ± 3.99	20.63 ± 2.322	26.10 ±3.99
WHR cm	0.82 ± 0.072	0.766 ± 0.058	0.87 ± 0.04
FBG mg/Dl	136.92 ± 55.50	88.28±13.36	190.84 ±29.53
Post Prandial mg/Dl	198.28 ± 46.99	160.92 ±24.23	238.72 ±30.19
HBA1C %	6.43 ± 1.61	5.20 ± 0.35	7.83 ±1.45
HDLC mg/Dl	40.72 ± 14.78	49.92 ±7.63	31.04 ±14.69
LDL mg/Dl	129.50 ± 27.67	107.96 ±18.50	153 ±11.53
VLDL mg/Dl	33.54 ± 15.15	20.68 ±6.52	47.36 ±8.19
TGL mg/Dl	179 ± 134.07	97.76±27.99	284.16 ±167.17
TC mg/Dl	293.42 ± 169.97	181.40 ± 3.59	426.28±176.42
NON- HDLC mg/Dl	139.90 ± 36.76	113.08 ±16.17	168.52 ±29.83
TROP I (pg/ml)	1091.43± 3483.8	2175.2 ± 4703.7	7.66± 4.56
BNP (peg /ml)	637.29 ± 1311.55	1217.5 ±1644.6	34 ±21.2
CKMB (mg/ml)	8.644 ± 10.828	14.94± 12.4	2.14 ± 1.426
Systolic BP (mm Hg)	140.45 ± 18	153.58 ± 18.46	128.2± 6.86
Diastolic BP (mm Hg)	84.38±12.78	95 ± 7.63	73.76 ± 6.46

*__BMI__: Body Mass Index; *__WHR__: Waist Hip Ratio; *__FBG__: Fasting Blood Glucose; *__HBA1C__: Glycosylated; Haemoglobin; *__TGL__: Triglycerides; *__TC__: Total Cholesterol; *__LDL__: Low-Density Lipoprotein; *__HDL__: High-Density Lipoprotein; *__BP__: Blood Pressure; *__CAD__: Coronary Artery Disease; *__SNP__: Single Nucleotide Polymorphism; *__TROP I__: Troponin I; __CK-MB__: Creatine kinase-MB; *__BNP__: Brain Natriuretic Peptide; *__OR__: Odds Ratio; *__SD__: Standard Deviation. *(Abbreviations used here also correspond to other tables where applicable.)*

The table shows dietary patterns of 50 individuals: 34% are vegetarians, 54% non-vegetarians, and 16% eggetarians. In the CAD group, 20% are vegetarians, 64% non-vegetarians, and 20% eggetarians, while the non-CAD group has 48% vegetarians, 44% non-vegetarians, and 13.6% eggetarians.

Table 2. Dietary Patterns of the participants.

Dietary pattern	N=50	%	Cad N=25	%	Non-cad N=25	%
Vegetarian	17	34%	5	20%	12	48%
Non- vegetarian	27	54%	16	64%	11	44%
Eggetarian	8	16%	5	20%	3	13.6%

The bar chart shows the frequency of different dietary habits among CAD subjects (N=25), with high salt diet and fast food being the most prevalent, followed by red meat and seafood. The dietary habits are further categorized into small, medium, and high frequency, with high salt diet being the most common in the high frequency group.

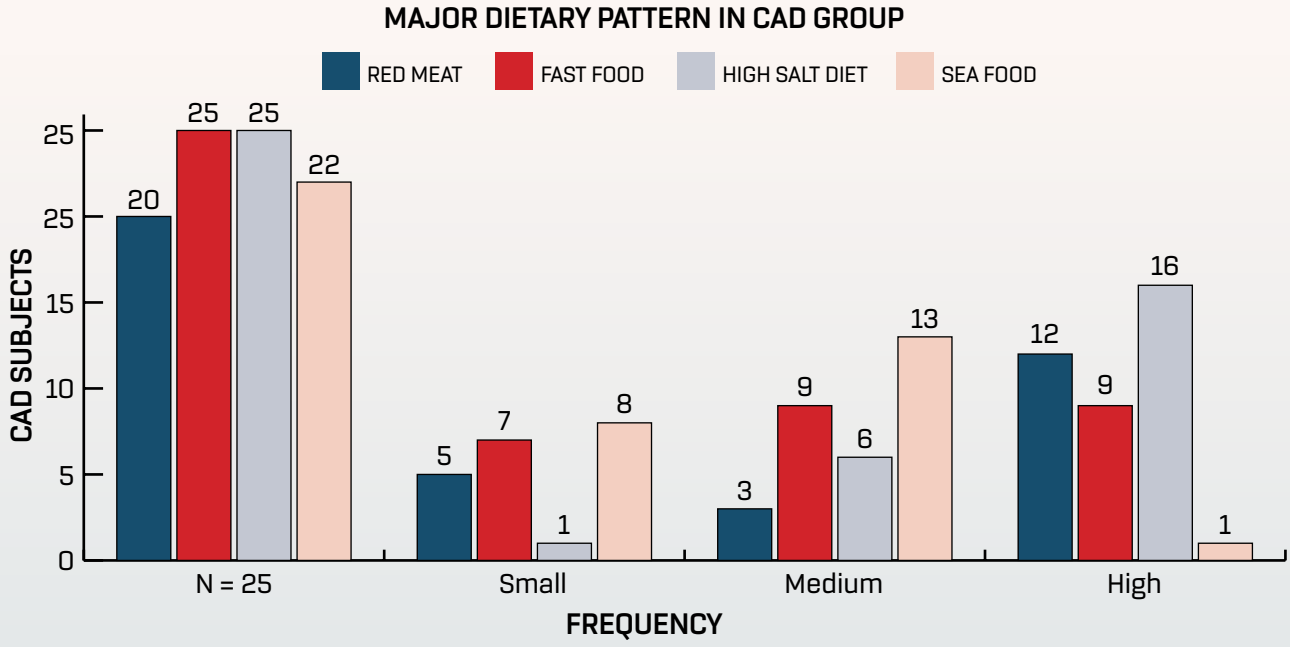

Figure 1. Major dietary pattern in CAD group.

The table shows Pearson correlation coefficients and p-values for cardiac markers with dietary factors such as red meat, fast food, seafood, and high salt intake. Significant correlations include HDL, LDL, VLDL, TGL, TC, and NON-HDLC with dietary components, while others like TROP-I, BNP, and CK-MB show non-significant associations.

Table 3. Correlation Analysis of biochemical parameters with dietary pattern among study articipants.

Cardiac marker	Pearson correlation	Red meat	Fast food	Sea food	High salt
TROP-I	r-value	0.077	-0.126	0.033	-0.014
	p-value	0.716	0.550	0.877	0.949
BNP	r-value	0.248	0.040	0.078	0.065
	p-value	0.232	0.848	0.709	0.757
CK-MB	r-value	0.091	0.236	-0.71	0.018
	p-value	0.665	0.256	0.736	0.931
HDL	r-value	-0.330	-0.327	-0.382	-0.112
	p-value	**0.02***	**0.003***	**0.05***	0.593
LDL	r-value	0.782	0.678	0.111	-0.078
	p-value	**0.02***	**0.01***	0.597	0.710
VLDL	r-value	0.868	0.764	-0.474	0.143
	p-value	**0.031***	**0.02***	**0.017***	0.495
TGL	r-value	0.891	0.678	-0.441	0.039
	p-value	**0.037***	**0.012***	**0.014***	0.853
TC	r-value	0.834	0.781	-0.228	-0.273
	p-value	**0.031***	**0.021***	0.273	0.186
NON-HDLC	r-value	0.718	0.151	-0.419	0.045
	p-value	**0.02***	0.472	**0.01***	0.833
Systolic BP	R-Value	0.141	0.025	0.035	0.618
	P-Value	0.452	0.913	0.733	**0.01***
Diastolic BP	R-Value	0.150	0.012	0.035	0.418
	p-value	0.521	0.812	0.733	**0.00***

Significant values are in bold*

The table shows the results of independent t-tests comparing clinical and biochemical parameters between CAD and non-CAD groups, with significant differences observed across all parameters ($p < 0.05$). Notably, parameters such as BMI, WHR, Troponin I, BNP, and various cholesterol levels exhibit substantial differences, highlighting the impact of CAD on these measures.

Table 4. Independent t-test of biochemical parameters between two groups.

Parameter	CAD group		Non-CAD group	
	T value	P value	T value	P value
BMI	7.607	**0.002**	7.506	**0.002**
WHR	6.370	**0.001**	6.216	**0.001**
TROP I	8.171	**<0.001**	8.171	**<0.001**
BNP	4.069	**<0.001**	4.069	**<0.001**
CKMB	4.853	**<0.001**	4.853	**<0.001**
Systolic BP	6.143	**<0.001**	6.143	**<0.001**
Diastolic BP	11.694	**0.000**	11.694	**0.000**
HDLC	5.701	**0.001**	5.701	**0.001**
LDLC	5.601	**<0.001**	5.601	**<0.001**
VLDLC	12.74	**0.002**	12.73	**0.002**
TGL	5.498	**<0.001**	5.498	**<0.001**
TC	6.905	**<0.001**	6.905	**<0.001**
NON-HDLC	8.171	**<0.001**	8.171	**<0.001**
HBA1C	8.805	**<0.001**	8.750	**<0.001**
FBS	10.04	**<0.001**	10.04	**<0.001**
Post Prandial	15.818	**<0.001**	15.818	**<0.001**

Significant values are in bold*

The table reveals significant differences between CAD and non-CAD groups in both lifestyle and sleep with significant p value <0.05.

Table 5. Independent t-test of non- biochemical parameters between two groups.

Variable	CAD group		Non-CAD group	
	T value	P value	Value	P value
Lifestyle	2.803	0.007	2.796	0.007
Sleep	4.387	0.000	4.394	0.000

Significant values are in bold*

The table below displays the frequency distribution of the ADIPOQ rs2241766 locus across study subjects, highlighting significant differences between CAD and non-CAD groups. The T:T genotype is notably absent in the CAD group but present in 26.9% of the non-CAD group, while the G:G genotype is more common in the CAD group (69.2%) than in the non-CAD group (7.7%). Additionally, allele frequencies vary significantly, with the T allele being predominant in the non-CAD group (56%) and the G allele more frequent in the CAD group (84%).

Table 6. Frequency distribution of the ADIPOQ rs2241766 locus across study subjects.

SNP site	Genotype /Allele	CAD group	NON-CAD group	P value
Rs2241766	T:T	0 (0.23)	7(26.9)	**<0.0001**
	T:G	7 (26.9)	23(88.5)	
	G:G:	18(69.2)	2(7.7)	
	T	8(0.16)	28 (0.56)	**0.0001**
	G	42(0.84)	28(0.56)	

Significant values are in bold*

The bar chart shows the frequency distribution of the ADIPOQ rs2241766 locus among study participants. The GG genotype and G allele were most common in individuals with coronary artery disease (CAD), followed by the TT genotype. Conversely, the TT and TG genotypes, as well as the T allele, were more prevalent in the non-CAD group compared to the CAD group.

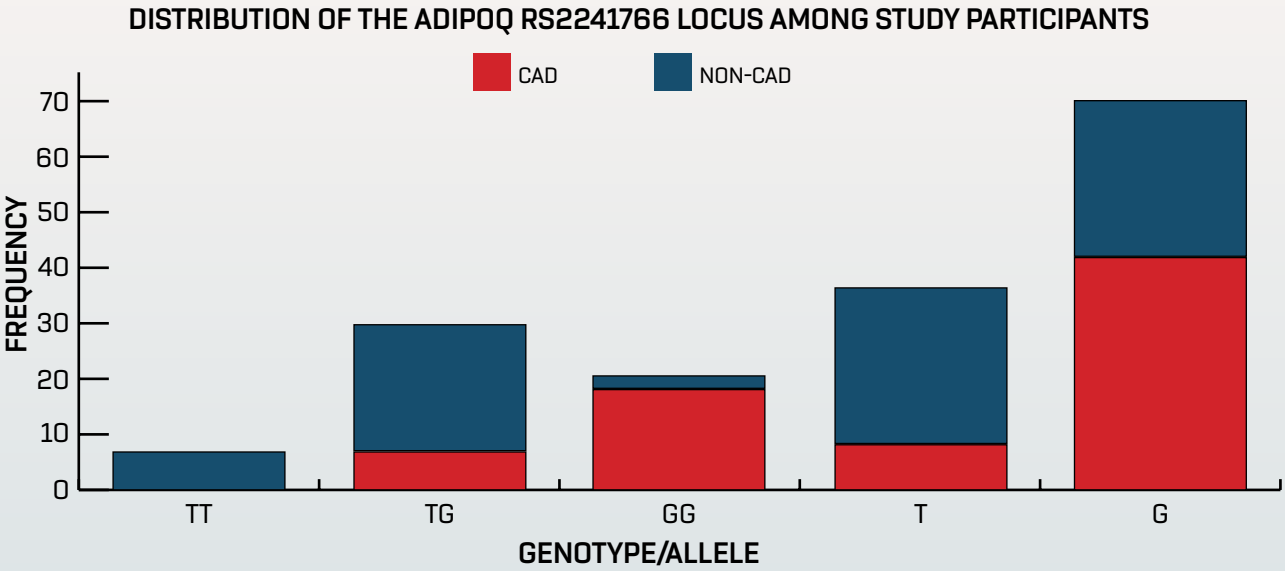

Figure 2. Distribution of the ADIPOQ rs2241766 locus among study participants.

In the CAD group, the GG genotype are much less likely to consume red meat compared to those without this genotype (OR<1). The statistically significant p-value (0.0182) and confidence interval (0.0085 to 0.6428) highlight a strong inverse association. While the GT genotype shows no significant. In the Non-CAD group, neither genotype demonstrated a significant effect with red meat.

Table 7. Interaction between genotypes and red meat consumption.

GROUP	GENE-DIET INTERACTION	OR	95%CL	P VALUE
CAD	GG VS RED MEAT	0.0741	0.0085 to 0.6428	**0.0182**
	GT VS RED MEAT	1.1953	0.3703 to 3.8582	0.7654
NON-CAD	GG VS RED MEAT	1.3788	0.4529 to 4.1973	0.5717
	GT VS RED MEAT	0.8366	0.2592 to 2.7004	0.7654

***CAD**: Coronary Artery Disease ***OR**: Odds Ratio ***CL**: Confidence Limit
(Abbreviations used here also correspond to other tables where applicable.)

Significant values are in bold*

In the CAD group, there was a notable association between the GG genotype and fast food consumption, whereas the GT genotype did not show a significant impact. In the Non-CAD group, neither genotype had a significant effect on fast food intake.

Table 8. Interaction between genotypes and Fast food consumption.

GROUP	GENE-DIET INTERACTION	OR	95%CL	P VALUE
CAD	GG VS fast food	0.0409	0.0077 to 0.2177	**0.0002**
	GT VS fast food	0.2188	0.0226 to 2.1137	0.1891
NON-CAD	GG VS fast food	0.3750	0.1058 to 1.3289	0.1286
	GT VS fast food	1.0000	0.3225 to 3.1006	1.0000

Significant values are in bold*

In the CAD group, a strong association was found between the GG genotype and high salt intake, while the GT genotype showed no significant effect. In the non-CAD group, neither genotype had a notable impact.

Table 9. Interaction between genotypes and high salt consumption.

GROUP	GENE-DIET INTERACTION	OR	95%CL	P VALUE
CAD	GG VS high salt	0.0247	0.0014 to 0.4511	**0.0125**
	GT VS high salt	0.2188	0.0226 to 2.1137	0.1891
NON-CAD	GG VS high salt	0.0036	0.1058 to 1.3289	0.1286
	GT VS high salt	1.6579	0.4051 to 6.7851	0.4820

Significant values are in bold*

The genotypes showed no significant effect on seafood consumption in either the CAD or Non-CAD groups.

Table 10. Interaction between genotypes and seafood consumption.

GROUP	GENE-DIET INTERACTION	OR	95%CL	P VALUE
CAD	GG VS seafood	0.2188	0.0226 to 2.1137	0.1891
	GT VS seafood	0.0625	0.0756 to 2.7550	0.3926
NON-CAD	GG VS seafood	1.6579	0.4051 to 6.7851	0.4820
	GT VS seafood	0.8512	0.2796 to 2.5912	0.7767

In the non-CAD group, a significant association was observed between the GT genotype and vegetarian diet, whereas the GG genotype had no significant effect. In the CAD group, neither genotype had a significant impact.

Table 11. Interaction between genotypes and vegetarian consumption.

GROUP	GENE-DIET INTERACTION	OR	95%CL	P VALUE
CAD	GG VS vegetarian	0.4565	0.0756 to 2.7550	0.3926
	GT VS vegetarian	3.5000	0.9206 to 13.3068	0.0660
NON-CAD	GG VS vegetarian	0.2188	0.0226 to 2.1137	0.1891
	GT VS vegetarian	5.6875	1.5098 to 21.4245	**0.0102**

Significant values are in bold*

In the CAD group, both the GG and GT genotypes were strongly associated with obesity, while in the non-CAD group, neither genotype showed a significant impact.

Table 12. Interaction between genotypes and obesity consumption.

GROUP	GENE-DIET INTERACTION	OR	95%CL	P VALUE
CAD	GG VS obesity	22.1538	2.5837 to 189.9581	**0.0047**
	GT VS obesity	5.1429	1.5220 to 17.3779	**0.0084**
NON-CAD	GG VS obesity	2.0870	0.1769 to 24.6160	0.5590
	GT VS obesity	1.7143	0.5245 to 5.6028	0.3724

Significant values are in bold*

DISCUSSIONS

In this study, the total sample size is 50 including 25 CAD and 25 non-CAD group. Descriptive statistical analysis was conducted on the study subjects and presented in Table 1. It shows that the sample was qualitatively heterogeneous with a broad age range and varying health conditions (such as abnormal glucose metabolism, poor lipid profiles, hypertension myocardial infarction and heart failure), which introduces variability in the primary data. The differences between the CAD and non-CAD groups are significant, emphasizing the need to interpret the findings with attention to the underlying health differences within the sample.

In Table 2, among the study subjects, the non-vegetarian group exhibited the highest prevalence, followed by the vegetarian and eggetarian groups. Specifically, in the CAD group, non-vegetarians were the most prevalent, followed by equal percentages of vegetarians and eggetarians. In contrast, in the non-CAD group, vegetarians were the most prevalent, followed by non-vegetarians and eggetarians, respectively. Utilizing the food frequency questionnaire (FFQ) to identify major dietary frequencies based on the highest consumption, four categories were delineated in (fig. 1). The “red meat-based” category, representing 80% of respondents, is characterized by a high intake of animal organ meats and fresh meat. The “fast food-based” category, constituting 100%, is typified by high-fat and high-carbohydrate items like burgers, fries, and sugary drinks. And “high salt-based diet” category involves frequent consumption of salt-rich foods like dry fish, pickles, pappads, fries, and chips. Lastly, the “seafood-based” category, representing 88%, encompasses various fish and shellfish varieties, including dry fish.

The study conducted correlation analysis, revealing significant associations between dietary habits and various health parameters. Specifically, high consumption of red meat and fast food showed positive correlations with LDL, VLDL, triglyceride (TGL), and total cholesterol (TC) levels, while displaying negative correlations with HDL levels. Conversely, seafood intake exhibited a positive correlation with HDL levels but negative correlations with TGL and VLDL levels. Moreover, a high-salt diet demonstrated positive correlations with systolic and diastolic blood pressure levels, as indicated in Table 3. Cahill LE et al. noted a strong link between fried food intake and type II diabetes mellitus, as well as moderate connections to coronary artery disease risk. These relationships were influenced by factors such as body weight, hypertension, and hypercholesterolemia (16).

The independent sample t-test demonstrated significant differences between CAD and non-CAD groups across various parameters, as outlined in Table 4. Babić Z. et al.’s findings indicate that patients with more narrowed coronary arteries tended to exhibit higher BMI and waist circumference. Furthermore, the waist-to-hip ratio showed associations with certain health markers with a significance level below 0.005, underscoring the study’s findings. Additionally, Alam et al. study found significant differences in serum cholesterol and HDL concentrations between Case and Control groups across all age groups ($P<0.0001$) in coronary heart disease patients proves the study (17, 18).

The independent T-test of lifestyle and sleep with CAD and non-CAD groups shows there is a significant difference in both lifestyle and sleep with $p<0.05$ given in Table 5.

The allele frequencies for the SNP in the ADIPOQ gene in both the CAD and non-CAD groups did not show significant deviation from Hardy-Weinberg equilibrium. Fisher’s exact test revealed a significant association between allele and genotype with CAD. In the genotype frequency distribution of the ADIPOQ gene in (Fig. 2), the TT wild-type was more prevalent in the non-CAD

group, while the GG mutant type was more common in the CAD group described in Table 6. This suggests that individuals with the GG genotype may have a higher risk of CAD compared to those with the TT genotype.

The results presented in Table 7 shows the link between genotypes and red meat intake in CAD and non-CAD groups. In the CAD group, the GG genotype was significantly less associated with red meat consumption (OR = 0.0741, 95% CI: 0.0085–0.6428, p = 0.0182), indicating that individuals with the GG genotype are less likely to consume red meat. The GT genotype showed no significant association (OR = 1.1953, p = 0.7654). In the non-CAD group, neither the GG nor GT genotypes were significantly linked to red meat intake. Janiszewska et al. discovered that increased intake of processed red meat may lower adiponectin levels, particularly among women, potentially mediated by BMI. This study underscores the link between diets high in red meat and saturated fats, such as typical Western diets, and reduced adiponectin levels (19).

In Table 9 and 10, there is a significant difference observed between the GG genotype and elevated intake of high-salt diet. However, no significant difference was found regarding seafood consumption and genotypes. The Table 11 demonstrate the potential link between the GT genotype and a vegetarian diet in non-CAD group, while no association was noted between GG genotype and vegetarianism in any group. This indicates a lower prevalence of the G allele among vegetarian consumers in the non-CAD group

Table 12 reveals that GG and GT genotypes were strongly linked to obesity in CAD group, while in the non-CAD group; neither genotype had a significant effect. Ogundele O. E., et al. studied ADIPOQ gene variations in young Nigerian adults, linking the rs266729 SNP to obesity indicators like BMI and waist circumference. The -11377G allele increased the risk of overall and abdominal fat, while the rs1501299 SNP showed no significant correlation with obesity measures (20). In non-CAD group, there is no significant association between genotypes and obesity.

Our study possesses several strengths and limitations. Notably, This South Indian study is pioneering in its exploration of the association between ADIPOQ genetic polymorphisms and dietary patterns in relation to CAD, marking a significant contribution to the field.

Nevertheless, the study is constrained by a relatively small sample size warranting larger studies for more robust results. Additionally, the cross-sectional design limits the assessment of temporal relationships, suggesting that a potential prospective study approach could yield more impactful findings. Furthermore, while our research focused on a single SNP, future investigations may benefit from exploring multiple SNPs to elucidate gene-gene interactions in larger populations.

CONCLUSIONS

The study explored the association between dietary patterns, genetic variations in the ADIPOQ gene, and obesity measures in CAD and non-CAD subjects. Dietary habits, including the consumption of red meat, fast food, seafood, and high-salt foods, showed significant correlations with lipid profiles and blood pressure levels. Furthermore, genetic variations in the ADIPOQ gene were associated with dietary preferences and obesity risk. Specifically, the rs2241766 GG genotype was linked to high red meat and fast-food consumption, while the GT genotype was associated with a vegetarian diet in the non-CAD group. In the CAD group, the GG and GT genotypes were significantly associated with obesity, indicating a potential genetic predisposition to obesity in CAD patients. These findings underscore the complex interplay between diet, genetics, and obesity in cardiovascular disease.

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CONFLICT OF INTEREST The authors declare no conflict of interest.

ETHICS APPROVAL Approval for this study was secured from the Ethics Committee of the Chettinad Hospital and Research Institute (approval ID: IHEC-I/2464/24).

CONSENT TO PARTICIPATE All participants in this study provided written informed consent.

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THE KNOWLEDGE, ATTITUDE AND PRACTICES OF PREGNANT WOMEN IN PREVENTING IRON DEFICIENCY ANEMIA IN GEORGIA

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ABSTRACT:

Introduction Anemia in pregnancy is a serious global health challenge, affecting, especially developing countries.

Materials and methods A qualitative research method was used to survey pregnant women with iron deficiency anemia (IDA) and physicians through in-depth interviews. The target sample consisted of 9 gynecologists and 26 pregnant women, selected through purposive sampling from three maternity hospitals in Tbilisi (Georgia).

Rezults The majority of pregnant women (n=22; 84.6%) knew IDA and correctly identified its symptoms. However, despite high awareness, most lacked adequate knowledge about the causes and risk factors of IDA. While pregnant women were aware of healthy eating practices, they did not follow a proper diet. Relevant obstacles to adopting a healthy eating pattern included limited financial access to food as well as cultural and religious barriers. Although the respondents had some knowledge about iron-rich foods, they were generally unaware of the need to take iron supplements for prevention. The majority of pregnant women (n=21; 80.8%) received little information about anemia from their family physicians, indicating the limited role of family doctors in preventing IDA during pregnancy.

Conclusions Although pregnant women have knowledge and positive attitudes regarding the prevention of IDA, the practice is unsatisfactory. The results indicate a weak link between knowledge about IDA prevention and healthy behavior, which is a major contributing factor to the prevalence of anemia. To solve the problem, it is necessary to encourage proper counseling on nutrition for pregnant women during antenatal care, with a key role played by family doctors. Raising awareness of the problem among women of reproductive age and adolescent girls should also be promoted.

Keywords Iron deficiency anemia (IDA), iron supplements, prevention, Georgia.

CUNOȘTINȚELE, ATITUDINILE ȘI PRACTICILE FEMEILOR ÎNSĂRCINATE ÎN PREVENIREA ANEMIEI FERIPRIVE ÎN GEORGIA

Introducere Anemia în timpul sarcinii reprezintă o provocare serioasă pentru sănătatea globală, afectând, în special, țările în curs de dezvoltare.

Materiale și metode A fost utilizată o metodă de cercetare calitativă pentru a chestiona gravidele cu anemie feriprivă (AF) și medicii prin intermediul unor interviuri aprofundate. Lotul țintă l-au constituit nouă ginecologi și 26 gravide, selectați prin eșantionare intenționată din cadrul a trei maternități din Tbilisi (Georgia).

Rezultate Majoritatea gravidelor (84,6%) aveau cunoștințe despre AF și identificau corect simptomele acesteia. Totuși, în pofida nivelului ridicat de conștientizare, majoritatea nu dețineau informații adecvate despre cauzele și factorii de risc ai AF. Deși gravidele erau conștiente de practicile alimentației sănătoase, acestea nu respectau o dietă corespunzătoare. Obstacolele relevante în adoptarea unui mod sănătos de alimentație îl constituiau accesul financiar limitat la alimente sănătoase, precum și barierele de ordin cultural și religios. Deși respondentele dețineau unele cunoștințe despre alimentele bogate în fier, majoritatea nu erau conștiente de necesitatea administrării suplimentelor de fier pentru prevenire. Majoritatea femeilor gravide (80,8%) au primit puține informații despre anemie din partea medicilor de familie, indicând un rol limitat al medicilor de familie în prevenirea AF în timpul sarcinii.

Concluzii Deși gravidele au cunoștințe și atitudini positive vizând prevenirea AF, situația în domeniu nu este satisfăcătoare. Rezultatele indică faptul că există o legătură slabă între cunoștințele despre prevenirea AF vs comportamentul sănătos, ceea ce reprezintă un factor determinant în prevalența anemiei. Pentru rezolvarea acestei probleme, este necesar să fie încurajată consilierea adecvată privind alimentația femeilor gravide în timpul îngrijirii prenatale, în care un rol decisiv îl joacă medicii de familie. Ar trebui, de asemenea, să fie promovată conștientizarea problemei în rândul femeilor de vârstă reproductivă și al fetelor adolescente.

Cuvinte cheie Anemie feriprivă, suplimente de fier, prevenire, Georgia.

INTRODUCTION

Iron deficiency anemia (IDA) in pregnancy is a condition in which the level of hemoglobin in the body of a pregnant woman decreases. The World Health Organization defines anemia as a condition when the hemoglobin level is below 11.0 g/dL during pregnancy and below 10.0 g/dL in the postpartum period (1).

Iron is essential for the production of red blood cells, which help carry oxygen throughout the body. If the number of red blood cells decreases, human organs and tissues do not receive as much oxygen as they need. There are two types of iron deficiency:

1) The hidden or latent type is characterized by reduced iron stores in the bone marrow, while the number of red blood cells and hemoglobin level remains normal;

2) IDA which is characterized by a decrease of all metabolic funds, and by a reduction of red blood cells and hemoglobin levels.

It should be emphasized that foods contain both heme and non-heme iron. Heme iron can be found in red meat, poultry, and fish (salmon, tuna, sardine). Non-heme iron can be found in nuts, cereals, spinach, and broccoli. Heme iron is a part of hemoglobin and myoglobin, and non-heme iron is stored in the human body as ferritin and delivered through the body via transferrin (2).

Despite iron's plentifulness on earth, people often experience its deficiency. Iron deficiency is the most widespread nutritional deficiency worldwide. In the developing world, iron deficiency occurs due to blood loss as a result of nutrient deficiencies or colonization with helminths, while in the developed world it occurs due to certain dietary behaviors (e.g., vegetarian diet and rejection of red meat) and pathological conditions (e.g., chronic blood loss or malabsorption) (3-6).

Iron deficiency causes severe consequences in children and pregnant women, as the demand for iron increases especially during pregnancy (7). If a pregnant woman has insufficient iron stores, IDA may develop. IDA in pregnant women can cause complications such as deterioration of perinatal and postpartum maternal health, growth retardation, and impaired cognitive and motor development in the newborn. IDA also increases the risk of maternal mortality and low birth weight (7).

Studies have proven that individual iron supplementation and proper nutrition are the best approaches to solving the problem of IDA (7). According to WHO recommendations, it is necessary to increase the daily dose of iron to 15 mg /day (approximately 30 mg/day). Daily iron and folic acid intake reduces the risk of maternal anemia by 70% and iron deficiency by 57%. Daily iron intake is recommended as part of antenatal care to reduce the risk of IDA, iron deficiency, and low birth weight.

It is worth noting that pregnant women should pay particular attention not to the quantity, but to the quality of their diet. A diet low in fat and carbohydrates and high in protein, calcium, iron, and vitamins is recommended. Iron-rich foods include legumes, green vegetables (especially spinach), bread, dried fruits, eggs, red meat, and fish (7,8).

According to the WHO, 27% of the world's population experience IDA (9). According to 2019 data, IDA occurs in 30-60% of pregnant women and is responsible for 22% of maternal deaths (10). The mortality of mothers and newborns caused by IDA globally amounts to an average of 2.5-3.5 million cases (11).

The World Health Organization adopted a global program to improve maternal and child nutrition, according to which the prevalence of anemia among women of reproductive age should be reduced by 50% by 2030 (12). It became clear that the prevalence of anemia was not declining as quickly as originally thought. A particularly high prevalence of IDA is observed among middle- and low-income pregnant women (13). According to 2023 data, 40.6% of pregnant women in Georgia had anemia at least once during pregnancy (14). The prevalence of anemia in pregnant women in Georgia is high compared to the global rate (37%) (15). In Georgia, the State Maternal and Child Health Program includes eight antenatal visits, and for all pregnant women with IDA, medication for iron deficiency anemia is provided free of charge (16).

Even though there are many methods for preventing IDA in pregnant women, the problem remains relevant and a large number of women experience health problems and complications associated with anemia. The risk factors causing IDA significantly depend on the awareness and attitude of pregnant women towards anemia, which, in turn, depends on the attitudes of primary health care specialist-obstetrician-gynecologist or family doctor (recognition of the importance of consultation). Therefore, it is believed that it is possible to reduce the prevalence of IDA by improving the level of education of pregnant women, as well as by changing the attitude and practical approach of family physicians and obstetricians-gynecologists regarding this problem (17).

To develop effective strategies to reduce the prevalence, it is necessary to assess the current perception and knowledge of pregnant women about variable risk factors for IDA. The first step towards solving this problem is to consider the weakest areas of knowledge and perceptions of pregnant women in the educational program.

This study aimed to explore the knowledge, attitudes, and perceptions of pregnant women regarding the prevention of IDA in Georgia.

MATERIALS AND METHODS

A phenomenological qualitative study was conducted to explore the experiences of pregnant women with IDA through in-depth interviews. The study included nine gynecologists and twenty-six pregnant women from three maternity hospitals in Tbilisi (Table 1).

Table 1: Demographic characteristics of pregnant women.

Characteristics	n=26	%
Age		
18-20	2	7.7
21-33	18	69.2
≥ 34	6	23.1
Number of children		
0	15	57.7
1	11	42.3
> 2		
Employment		
Housewife	7	26.9
Self-employed	5	19.2
Employed	14	53.8

Characteristics	n=26	%
Education		
Secondary education	9	34.6
Bachelor	13	50
Master	4	15.4
Income status		
250 GEL	3	11.5
250-500 GEL	3	11.5
500-800 GEL	9	34.6
>800 GEL	11	42.3
Gestational age	15	57.7
≤12 weeks	11	42.3
≥12 weeks		

Pregnant women were initially invited to participate by a nurse. With the consent of pregnant women to participate in the survey, a face-to-face meeting was held in the polyclinic departments of maternity homes during working hours from 11 am to 3 pm.

Women interested in participating in the study were fully informed by the researcher about the objectives, process, and ethical issues of the study. After providing written consent, the participants were selected. The inclusion criteria were the pregnant women diagnosed with IDA without any complications. Data were collected through individual in-depth interviews with obstetricians-gynecologists and pregnant patients between March and July 2024. The interviews with each participant lasted approximately 35 to 50 minutes.

The study utilized a semi-structured interview guide to collect qualitative data from participants. The questionnaire consisted of open-ended questions that explored various aspects of pregnant women's experiences with IDA, including their knowledge, perceptions, dietary habits, and adherence to medical recommendations. The interview guide included approximately 10-15 core questions, with additional follow-up questions depending on the participant's responses to allow for a deeper exploration of their experiences. This approach ensured consistency while providing flexibility to capture rich, detailed insights.

During the interviews, a voice recorder was used to capture audio recordings. Afterward, the interviews were transcribed into a written format, and the transcripts were carefully reviewed and verified for accuracy. The transcripts were read multiple times to gain a deeper understanding of each interview.

For data analysis, thematic analysis was applied due to its flexibility, making it particularly suitable for qualitative studies. This process involves six stages: a) Familiarizing with the data by reading and identifying key concepts and patterns, b) Generating initial codes, c) Organizing these codes into themes, d) Reviewing and refining the generated themes, e) Defining and naming the themes, f) Producing a comprehensive data analysis report.

ETHICAL ISSUES

Consent to conduct the research was obtained from the Ethics Council of the Caucasus University (CAU No. 012/23). The respondents were informed in advance about the study's objectives. The questionnaires emphasized the strict protection of research confidentiality. Pregnant women decided to participate in the study voluntarily, without any pressure.

Pregnant women could refuse to participate in the study at any time without providing any reason. All the study data were identified by individual codes. The data were presented without personal identification.

RESEARCH LIMITATIONS

The study was conducted only in randomly selected maternity hospitals. Therefore, it is not appropriate to generalize the results. Additionally, one of the limitations of the study was the lack of statistical data and literature on the prevalence and prevention of IDA in Georgia.

RESULTS

RESULTS OF A SURVEY OF OBSTETRICIAN-GYNECOLOGISTS

Causes of IDA in Pregnancy

The doctors named the worsening socioeconomic situation as one of the reasons for the increase in the prevalence of inadequate nutrition and anemia. Pregnant women cannot afford many expensive foods, which has become one of the causes of IDA.

"This is the most common situation in our reality. About 80% of my pregnant patients are anemic. Cases of anemia have increased significantly in recent years. It should be noted that in the 80s and 90s of the last century, anemia was less common than now. In my opinion, the reason for this is a change in diet. Previously, pregnant women consumed a lot of meat and fat, and meat, as is widely known, helps prevent IDA, but increases the risk of overweight and hypertension. Now the opposite is true, due to socioeconomic problems, pregnant women primarily consume vegetarian foods, which protect against hypertension, but increase the prevalence of anemia".

1st gynecologist.

One of the gynecologists named the short interval between pregnancies and especially multiple pregnancies as the main cause of IDA.

"*During pregnancy, conditions conducive to anemia are created. The mother's body supplies the fetus with the substances it needs, including iron. With repeated pregnancies after a while, iron stores in the mother's body cannot be restored, and this is one of the leading causes of IDA".*

2nd gynecologist.

According to one of the gynecologists, the increased prevalence of IDA is the result of environmental problems (for example, increased levels of radiation), poor food quality, stress, and unstable economic and marital status.

"*Most of the imported products are expired and contain harmful, toxic substances."*

3rd gynecologist.

Knowledge of IDA and adherence to its prevention methods

Some doctors expressed satisfaction with the general awareness of pregnant women about proper nutrition. In their opinion, pregnant women usually follow the advice as much as possible. However, most of them are not satisfied with the adherence of pregnant women to medical recommendations, citing socioeconomic difficulties as the main reason.

"Women read a lot and come to my clinic with basic knowledge about healthy eating."

4th gynecologist.

"When I give my pregnant patients advice on proper nutrition, they are silent and just look at me. How can we afford all these products? "

5th gynecologist.

"The state program for pregnant women does not include free iron supplements, this is why most pregnant women do not want to buy iron supplements for financial reasons."

6th gynecologist.

Preventive methods of IDA

Although doctors prescribe iron supplements and a proper diet to pregnant patients to prevent IDA, the problem still exists. According to most doctors, it is advisable to distribute free iron supplements and prenatal vitamins to pregnant women in maternity hospitals and women's outpatient clinics. Doctors believe that preventive iron replacement therapy is ineffective without properly informing pregnant women.

"If a pregnant woman is unaware of the risk of IDA, she doesn't even want to take vitamins. Therefore, in any case, it is necessary to inform patients about the importance of iron supplements."

7th gynecologist

"Sometimes we have a long line of pregnant women waiting for a consultation and we simply don't have time to talk to every pregnant patient about nutritional issues. We have brochures about lactation that we printed for our patients which make things easier for us. Of course, we emphasize the need for breastfeeding when talking to a pregnant woman, but the patient can find more information and answers to questions in this brochure. It would be beneficial to create similar informative brochures on healthy eating during pregnancy, especially in terms of preventing IDA, as the latter is a serious problem in today's reality."

8th gynecologist

Most doctors welcome the opinion that increasing the level of education of pregnant women and changing their attitude toward iron supplements will help fight IDA and find a way out of the situation. However, they noted that improving the socioeconomic situation was necessary to solve the problem.

The role of the family physician in the prevention of IDA.

According to gynecologists, it is necessary to involve a family physician and a gynecologist in the process of managing IDA in pregnant women. In this regard, a family doctor's involvement in the process of preventing IDA in Georgia is one of the main tasks.

"There has been a trend in the country where pregnancy is managed solely by gynecologists, who also address several related issues, including IDA. Family doctors are less involved or, in many cases, do not participate in this process and do not assume this responsibility."

9th gynecologist

RESULTS OF A SURVEY OF PREGNANT WOMEN

Knowledge and perceptions of pregnant women about anemia

Most pregnant women interpreted anemia as a "lack of blood". Only four respondents with higher education knew the medical definition of "anemia". A possible reason for ignorance of medical terminology may be the low level of general education or the infrequent use of medical terminology by healthcare professionals when communicating with patients.

"I don't know exactly what the word "anemia" means. I first heard about it from a gynecologist."

A 21-year-old mother in her first pregnancy, self-employed, Secondary education, 250-500 GEL, ≤12 weeks

Pregnant women identified gynecologists, the internet, television, books, family physicians, mothers, and relatives as sources of information about anemia.

"Yes, I have heard that anemia means a lack of blood in the body, which is very common during pregnancy. The doctor advised me to run a blood test as he told me that the red blood cell count was low and I had reduced hemoglobin levels."

A 22-year-old mother with one child, employed, Bachelor degree, 500-800 GEL, ≥12 weeks

Respondents primarily described anemia for its symptoms, such as general weakness, mild fatigue, decreased appetite, nausea and vomiting, aversion to certain foods, pallor of the skin, and conjunctiva, "black circles under the eyes", "dizziness", "fainting", "white lines on the nails".

Twelve respondents experienced mild to moderate weakness during pregnancy, and some experienced dizziness; However, due to the mild course, none of them consulted a doctor. Anemia is not a serious condition, according to some respondents, as anemia-related weakness and dizziness are "normal during pregnancy."

"Fatigue and weakness are part of pregnancy. It doesn't affect the mother or her baby".

A 23-year-old mother with two children, employed, Master's degree, >800 GEL, ≤12 weeks

"A pregnant woman carries Another life inside her. It's something new for her body, and she may get tired because of it, or she may have dizziness and other symptoms."

A 21-year-old mother with one child, self-employed, Secondary education, 250-500 GEL, ≤12 weeks.

"Feeling nauseous and disgusted with certain foods during pregnancy is natural. Gradually, the pregnant woman adapts to these symptoms."

A 22-year-old mother with two children, Employed, Bachelor, >800 GEL, ≤12 weeks

Respondents' perception of anemia as a "normal phenomenon of pregnancy" was also supported by the fact that women of reproductive age shared similar experiences in social networks. In their opinion, anemia was a natural part of pregnancy, because at this time changes occurred in the body that did not cause any harm to either the child or the mother.

"If other women, despite these symptoms, can give birth normally and safely, then why take it seriously?"

A 27-year-old-woman with two children, self-employed, Secondary education, 250-500 GEL, ≤12 weeks

According to the respondents, the symptoms of anemia can be eliminated by resting and eating certain foods.

"I often experience fatigue, dizziness, and weakness during pregnancy. My mother tells me that this is natural during pregnancy. I rest at such times. I feel good after resting."

A 25-year-old mother with two children, Employed, Bachelor degree, >500-800 GEL, ≤12 weeks

However, if pregnant women experienced severe weakness, fever, abdominal pain, white vaginal discharge, or bleeding, they understood, that these symptoms could have a severe impact on the baby and usually consulted a doctor.

"Bleeding can harm the baby, because it won't have enough blood supply, and it can interfere with the development of my son. Bleeding can also cause premature birth or miscarriage."

A 27-year-old-woman with two children, self-employed, Secondary education, 250-500 GEL, ≤12 weeks

"Abdominal pain is a dangerous sign because the baby is growing in my belly and everything that affects me will affect my baby; Therefore, in case of abdominal pain, you should immediately consult a doctor."

A 23-year-old mother with two children, Employed, Master degree, >800 GEL, ≤12 weeks

IDA: Causes

The majority of respondents noted that the main causes of anemia during pregnancy are insufficient, unbalanced, and low-quality nutrition, sharing blood with the fetus, increased energy consumption, emotional stress, long exposure to the sun, and physiological factors.

Although the respondents mentioned various causes of anemia, almost none of them had accurate knowledge of its etiology.

"During pregnancy, we need extra nutrition because we are sharing blood with our baby. Therefore, we should eat more vegetables to increase our hemoglobin levels."

A 24-year-old mother with one child, Employed, Bachelor degree, >500-800 GEL, ≤12 weeks

"When a woman does not follow a proper diet and has emotional problems, does not walk outdoors every day – all of this can contribute to the development of anemia."

A 21-year-old mother in her first pregnancy, Self-employed, Secondary education, 250-500 GEL, ≤12 weeks

"Anemia can be caused by the lack of a balanced diet containing essential nutrients that can maintain the necessary volume of blood in the body."

A 20-year-old mother with one child, employed, bachelor's degree, >500-800 GEL, ≥12 weeks

"Anemia is especially common during pregnancy because a new life is developing inside a woman and therefore she needs more energy and strength."

A 27-year-old-woman with two children, Self-employed, Secondary education, 250-500 GEL, ≤12 weeks

"Prolonged exposure to the sun during working hours and tedious work can lead to a decrease in the amount of blood in the body."

A 21-year-old mother with two children, self-employed, Secondary education, 250-500 GEL, ≥12 weeks

"Pregnancy can cause anemia because the fetus receives blood from the mother, meaning the blood volume of the fetus depends on the mother's blood. This is how the mother passes on some of her blood to the fetus".

A 19-year-old mother with one child, self-employed, Secondary education, 250-500 GEL, ≥12 weeks

The role of food in the prevention of IDA

Respondents unanimously stated that the most effective way to prevent anemia in pregnant women was to maintain a healthy diet, with medications playing a secondary, supportive role. By their definition, a healthy diet is "nutrient-rich"; "High-calorie", "consisting mainly of dairy products, vegetables and fruits", and "vitamin-rich nutrition."

Most of the study participants said pregnant women should eat foods such as fruits, vegetables, meat, milk, dairy products, and natural juices since healthy food "gives energy and strength to a pregnant woman", which "increases the amount of blood in the body."

"In my opinion, eating properly during pregnancy is more important than ever. We need more fruit and vegetables, we need to eat meat, drink milk, and eat more dairy products and natural juices, because healthy food "gives energy and strength to a pregnant woman", and "increases the amount of blood in the body. It is necessary to eat only healthy food every day, which will give the child all the important nutrients. Also, a healthy diet will contribute to the birth of a child with a normal weight."

A 27-year-old mother with two children, Employed, Master degree, 500-800 GEL, ≤12 weeks

"We should eat foods that can increase blood volume and raise hemoglobin levels, such as red meat, beans, honey, walnuts, pomegranate juice, and more. Doctors teach us to eat properly. We must follow their instructions to improve."

A 22-year-old mother with two children, Employed, Bachelor degree, >800 GEL, ≤12 weeks

"I try to make my diet as diverse as possible. A pregnant woman's diet is unimaginable without dairy products as a source of protein and calcium. Also, taking 1-2 tablespoons of red wine a day improves the hemoglobin index."

A 23-year-old mother with two children, Employed, Master degree, >800 GEL, ≤12 weeks

When asked if the diet of pregnant women should be different from that of non-pregnant women, the majority of pregnant women answered positively, but the answers to what should be the diet of a pregnant woman varied.

"One of the peculiarities of pregnancy is that a pregnant woman may want to eat something different, even strange. Therefore, she must satisfy her desire and eat what she wants. The happier the expectant mother is, the more likely she is to give birth to a healthy child. For example, I have a strong desire to eat pickles and Staphylea, although I know it is not recommended to eat these foods during pregnancy."

A 21-year-old mother in her first pregnancy, self-employed, Secondary education, 250-500 GEL, ≤12 weeks

"It's important to me to eat the foods I want during pregnancy, even though my doctor recommends other foods to prevent anemia."

A 19-year-old mother in her first pregnancy, employed, bachelor's degree, 500-800 GEL, ≥12 weeks

Most pregnant women were more or less satisfied with their diet. They reported that they increased the amount of meat, dairy, fruit, and vegetables in their diet during pregnancy.

"I am satisfied with my diet. I believe that I have an optimal diet for my condition."

A 22-year-old mother with one child, Employed, Bachelor degree, 500-800 GEL, ≥12 weeks

Although pregnant women had adequate knowledge about healthy eating, they did not follow the necessary, correct diet. Their daily intake of necessary food was unstable. According to several pregnant women (7 out of 26), their diet would be more diverse if they had a better financial situation. One of the obstacles to a healthy diet is the high price of food products and less financial access:

"We have to eat a lot of vegetables and fruit during pregnancy, but with food prices rising, it's impossible to eat good food every day."

A 22-year-old woman pregnant with a second child, Employed, Bachelor degree, >800 GEL, ≤12 weeks

"If I don't have the money, how can I eat good and healthy food?"

A 29-year-old mother of two children, self-employed, Secondary education, 250-500 GEL, ≥12 weeks

However, cultural barriers also affect the nutrition of pregnant women. Some women (7 out of 26) relied on a vegetarian diet because of their religious orientation. They also noted that the responsibilities of caring for other family members made it difficult to maintain a healthy diet during pregnancy.

"Being responsible for family members makes it difficult to look after yourself. It's very different when you're in your mother's house, where you can spend more time on yourself and do whatever you want."

A 21-year-old mother in her first pregnancy, self-employed, Secondary education, 250-500 GEL, ≤12 weeks

"I have a mother-in-law and another child at home and I have to look after them, cook for them, and do other things. I get very tired. Sometimes I can't eat on time."

A 24-year-old mother with one child, Employed, Bachelor degree, 500-800 GEL, ≤12 weeks

According to pregnant women, it is necessary to get more information about "diet and food composition".

"*We would like to know more about the foods that are recommended during pregnancy."*

A 21-year-old mother in her first pregnancy, self-employed, Secondary education, 250-500 GEL, ≤12 weeks

Knowledge of pregnant women about foods containing iron and folic acid

Almost every woman has heard the terms "iron" and "folic acid". They had some idea about foods containing iron, but most of the respondents did not know that the cause of anemia is iron deficiency in their bodies. Also, none of the pregnant women knew about foods containing folate.

"Iron is found in fruits, green vegetables, eggs, meat, and fish."

A 21-year-old mother in her first pregnancy, self-employed, Secondary education, 250-500 GEL, ≤12 weeks

"Foods like fruits and vegetables, especially green vegetables, contain iron."

A 26-year-old mother with one child, Employed, Bachelor, >800 GEL, ≥12 weeks

"I don't know any food that is high in folate, it can only be taken as a medicine."

A 22 -year-old-mother in her first pregnancy, employed, Secondary education, 250-500 GEL, ≤12 weeks

Knowledge and attitudes of pregnant women toward iron-folic acid supplementation

Almost all respondents had some idea about iron and folic acid supplements. However, only five women identified iron deficiency as a cause of anemia.

The respondents reacted positively to iron preparations for the prevention of IDA. Taking iron and folic acid drugs has a positive effect on women and chil-

dren's health, "empowers" and is useful for "preventing frailty in women", especially during pregnancy, they said.

"Yes, I know that women should take these supplements during pregnancy – because after taking them, the body feels better, and they help a mother and a growing child to be strong and healthy."

A 21-year-old woman in her first pregnancy, employed, Bachelor degree, 500-800 GEL, ≥12 weeks

"Women should take iron and folic acid supplements during pregnancy to stay healthy and strong. It helps you to have a healthy baby."

A 20-year-old woman in her first pregnancy, employed, Bachelor degree, >800 GEL, ≥12 weeks

"I know that iron and folic acid supplements have a positive effect on women's health, especially during pregnancy. It promotes blood production and prevents anemia during pregnancy."

A 20-year-old woman with one child, employed, Bachelor degree, >800 GEL, ≤12 weeks

Some of the interviewed pregnant women (12 out of 26) regularly took iron and folic acid supplements. Respondents explained their regular use of these supplements by the fact that health professionals convinced them of their positive impact on the physical and mental development of the child.

They also believed that supplements should be good for the baby because "doctors know best what is best for pregnant women":

"*The doctor explained that these supplements will help my child's mental development. I trust my doctor. By taking these supplements, my child will be born healthy."*

A 26-year-old mother with one child, Employed, Bachelor, >800 GEL, ≥12 weeks

"*My dream is to have a healthy child. For my child to be born healthy, I must take supplements regularly. However, you cannot rely on medication alone. There should be a balance between healthy eating and medication."*

A 21-year-old woman in her first pregnancy, employed, Bachelor degree, 500-800 GEL, ≥12 weeks

A small part of the surveyed pregnant women (6 out of 26) did not want to take any medication during pregnancy at all. According to them, if the diet is rich and varied, there is no need to take additional iron preparations to prevent IDA.

"*Eating healthy food is more important than taking medicines because nutrition is the body's natural way of development."*

A 22-year-old woman with one child, employed, Bachelor degree, 500-800 GEL, ≥12 weeks

"It is quite possible that iron tablets are more harmful. I can fight anemia with proper nutrition - by taking iron-containing products."

A 21-year-old mother in her first pregnancy, self-employed, Secondary education, 250-500 GEL, ≤12 weeks

"I prefer to avoid taking any medication during pregnancy as much as possible and iron supplements are no exception."

A 22-year-old woman in her first pregnancy, employed, Bachelor degree, 500-800 GEL, ≥12 weeks

"Now my son needs good nutrition. So, I will only take the medicine if it has a good effect on my child's growth."

A 24-year-old mother with one child, employed, Bachelor degree, >500-800 GEL, ≤12 weeks

These women were unaware of the health problems that could occur if they did not take iron and folic acid supplements before and during pregnancy. However, some pregnant women have reported that if they do not take these supplements, the growing child may have physical or mental health problems.

"If women don't take these supplements during pregnancy, they will be physically weak. Not taking supplements harms a child's health, especially their physical or mental health."

A 22-year-old mother in her first pregnancy, employed, Bachelor degree, 500-800 GEL, ≥12 weeks

Most pregnant women were not aware of the recommended dose of iron and folic acid preparations, which might be due to their low education levels.

Adherence of pregnant women to iron and folic acid supplementation

Some of the pregnant women in the study reported not knowing when women should start taking these supplements. This shows that some health professionals do not provide their pregnant patients with adequate information about iron and folic acid supplements.

"I don't know exactly when pregnant women should start taking iron and folic acid supplements, but I know women should start taking them when they get pregnant."

A 19-year-old woman in her first pregnancy, employed, bachelor's degree, 500-800 GEL, ≥12 weeks

Only a few pregnant women knew about the need to start taking these supplements before pregnancy.

"*Women should start taking iron and folic acid preparations early in pregnancy, preferably months before pregnancy."*

A 20-year-old women in her first pregnancy, employed, bachelor's degree, >800 GEL, ≤12 weeks

Most participants did not know why pregnant women should take iron and folic acid supplements before pregnancy.

"I know why women should start taking these supplements before pregnancy. If women do not take preventive measures before pregnancy, the baby may be born weak mentally and physically."

A 22-year-old mother with two children, employed, Bachelor degree, >800 GEL, ≤12 weeks

DISCUSSION

According to doctors, the main causes of IDA are inadequate nutrition, poor quality food, environmental problems (for example, increased radiation levels), stress and unstable economic conditions. According to doctors, although pregnant women are more or less informed about proper nutrition, they do not follow medical recommendations, which is caused by socio-economic difficulties. According to gynecologists, the family doctor is less involved in the management of IDA in pregnant women and does not take responsibility. This is because primary health care is poorly developed in Georgia (18).

Involvement of the family doctor is seen as one of the key tasks for the prevention of IDA. Doctors believe that it is necessary to distribute iron supplements and prenatal vitamins to pregnant women free of charge in maternity hospitals and women's outpatient clinics. In addition, it is necessary to raise the level of education of pregnant women and change their attitude towards iron supplements, however, to solve the problem, it is necessary to improve the socio-economic situation.

Gynecologists play a critical role in preventing IDA as they see pregnant women eight times during pregnancy. They can improve prevention by:

- Early Screening & Monitoring – Regular hemoglobin and ferritin level checks.
- Patient Education – Reinforcing dietary guidance and addressing misconceptions about iron supplements.
- Ensuring Compliance – Monitoring adherence to supplementation and addressing barriers.
- Collaboration with Family Doctors – Enhancing primary care involvement for continuous support.
- Advocating for Free Supplements – Supporting policies for free iron and prenatal vitamin distribution.
- Prevention Programs – Implementing educational initiatives in hospitals and communities.

A total of 84.6% of pregnant women correctly identified the symptoms of IDA. The relatively high awareness of anemia among them may be attributed to the socio-economic characteristics of the study participants. Our study was conducted among urban pregnant women who might have adequate knowledge about anemia. Similar results were obtained from other studies (19,20). However, despite such high awareness, a total of 82.3% of the respondents did not know the clinical term of anemia, the causes, and the risk factors of IDA. Respondents defined anemia as a "lack of blood supply" in the body, which is a "normal, natural" condition during pregnancy, does not cause any harm to the child or the mother, and does not require medical attention. These perceptions of anemia indicate that, despite information and educational efforts by governmental and non-governmental organizations, pregnant women's understanding of anemia has changed little in recent decades (21). The high prevalence of anemia in pregnant women further reinforces the perception that "anemia during pregnancy is normal".

The respondents unanimously stated that the best preventive method for anemia is a healthy diet. Despite this knowledge, the respondents did not follow proper nutrition guidelines. Their daily intake of essential food was unstable. They had some idea of iron-containing foods, but most of those surveyed were unaware that iron deficiency was the cause of the anemia. Also, none of the pregnant women knew about products containing folic acid, which is related to the fact that folic acid is usually considered medicine by pregnant women. Similar results have been observed in other studies (22,23).

In our study, 78.3% of pregnant women demonstrated good awareness of anemia prevention strategies. Despite awareness of healthy eating, respondents did not adhere to the correct dietary pattern. Their daily intake of necessary food was unstable. One of the obstacles to a healthy diet was the rising cost of food making it less affordable. Cultural barriers also affect the nutrition of pregnant women. Due to religious or cultural values, some pregnant women followed a vegetarian diet that reduced iron intake through meat products. They also noted that the responsibility of caring for other family members made it difficult to maintain a healthy diet during pregnancy, suggesting the need to involve family members in efforts to reduce anemia.

In our study, 76.3% of pregnant women held misconceptions about anemia prevention methods. They believed that it is possible to correct and control IDA only with proper nutrition, with no need for iron supplements. According to them, if the diet is rich and varied, there is no need to take additional iron preparations to prevent IDA. They were also concerned that iron preparations, like other medications, could negatively affect the fetus. Many of them knew little about the potential health problems that could arise if they did not take iron-containing supplements, which may be attributed to their lower educational levels.

Studies have shown that doctors spend less time counseling pregnant women about IDA. A total of 81.2% of pregnant women find information mainly through the Internet, television, or literature, the rest receive information mainly from gynecologists. It is worth noting that only one of the interviewed pregnant women received counseling about IDA from a family physician, which indicates the limited role of a family physician in the prevention of IDA.

CONCLUSIONS

Despite some knowledge about the causes and prevention of IDA, its prevalence remains high in Georgia. This suggests that there is no link between the awareness of anemia and the adoption of healthy behaviors required to reduce its incidence. This highlights the complexity of perceptions regarding the causes of anemia and the need for an integrated approach to address the issue. Such an approach would involve improving prevention methods, ensuring more active involvement of family physicians, and enhancing government recommendations and nutrition programs for pregnant women. It is recommended to distribute iron supplements to pregnant women free of charge in maternity hospitals and women's outpatient clinics.

Although knowledge is essential, it is not sufficient to change the behaviors needed to improve health outcomes. In this context, greater public engagement and effective policy intervention can play a crucial role in overcoming existing challenges.

CONFLICT OF INTEREST The authors declare no conflicts of interest.

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SEROPREVALENCE OF HEPATITIS E VIRUS IN FIVE HIGH-RISK POPULATIONS FROM THE REPUBLIC OF MOLDOVA: A CROSS-SECTIONAL STUDY

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SUMMARY

Introduction The study has assessed the seroprevalence of Hepatitis E virus (HEV) markers in different at-risk groups within the Republic of Moldova. The risk groups included blood donors, hemodialysed patients, medical workers, tuberculosis (TB) patients, and intravenous drug users (IDUs).

Materials and methods A cross-sectional descriptive-epidemiological study was conducted from 2019 to 2023, with participants randomly selected from different risk groups. Blood samples were collected and tested using ELISA for Anti-HEV IgG and IgM markers. Seroprevalence was calculated with 95% confidence intervals, and statistical analyses were conducted using Epi Info 7.2 software.

Rezults Among 794 tested blood donors, 9.6% (95% CI: 7.7-11.8) were positive for Anti-HEV IgG, indicating past exposure, and 8.3% (95% CI: 6.3-10.8) for Anti-HEV IgM, suggesting recent infection. Hemodialyzed patients had a significantly higher seroprevalence: 45.8% (95% CI: 34.8–57.1) for Anti-HEV IgG and 21.6% (95% CI: 9.8–38.2) for Anti-HEV IgM. Medical workers exhibited moderate IgG prevalence at 11.8% (95% CI: 9.1-15.0) and substantially higher IgM prevalence at 38.1% (95% CI: 26.1-51.2). TB patients had lower IgG (11.9%, 95% CI: 7.8-17.2) and IgM (7.8%, 95% CI: 3.6-14.3) prevalences. IDUs had a notable IgG prevalence of 20.5% (95% CI: 12.6-30.4) but no detectable IgM.

Conclusions This study highlights the significant burden of hepatitis E virus infection among at-risk populations in the Republic of Moldova.

Keywords Hepatitis E virus, Moldova, risk groups, anti-HEV antibodies, seroprevalence.

SEROPREVALENȚA VIRUSULUI HEPATITIC E ÎN CINCI POPULAȚII CU RISC RIDICAT DIN REPUBLICA MOLDOVA: UN STUDIU TRANSVERSAL

Introducere Studiul a evaluat seroprevalența markerilor virusului hepatitei E (VHE) în grupuri de risc din Republica Moldova: donatori de sânge, pacienți hemodializați, lucrători medicali, pacienți cu tuberculoză (TB) și utilizatori de droguri intravenoase (UDI).

Materiale și metode Între 2019 și 2023, s-a efectuat un studiu transversal descriptiv-epidemiologic, cu participanți selectați aleatoriu. Probele de sânge au fost analizate prin ELISA pentru Anti-HEV IgG și IgM. Seroprevalența a fost calculată cu intervale de încredere de 95%, iar analizele statistice au fost efectuate cu Epi Info 7.2.

Rezultate Dintre cei 794 de donatori de sânge, 9,6% (IC 95%: 7,7-11,8) au fost pozitivi pentru Anti-HEV IgG și 8,3% (IC 95%: 6,3-10,8) pentru Anti-HEV IgM. Pacienții hemodializați au prezentat seroprevalențe mai mari: 45,8% (IC 95%: 34,8-57,1) pentru IgG și 21,6% (IC 95%: 9,8-38,2) pentru IgM. La lucrătorii medicali, prevalența IgG a fost de 11,8% (IC 95%: 9,1-15,0), iar cea a IgM de 38,1% (IC 95%: 26,1-51,2). Pacienții cu TB au avut prevalențe de 11,9% (IC 95%: 7,8-17,2) pentru IgG și 7,8% (IC 95%: 3,6-14,3) pentru IgM. UDI au prezentat o prevalență de 20,5% (IC 95%: 12,6-30,4) pentru IgG, fără IgM detectabil.

Concluzii Studiul nostru relevă severitatea infecției cu virusul hepatitis E în grupurile de risc din Republica Moldova.

Cuvinte cheie Virusul hepatitei E, Moldova, grupuri de risc, anticorpi anti-HEV, seroprevalență.

INTRODUCTION

Hepatitis E virus (HEV) infection is a significant global public health concern, affecting both developed and developing nations, with approximately 20 million infections annually, including 3.3 million symptomatic cases (1).

Although often considered a self-limiting illness, HEV can result in severe outcomes, particularly in immunocompromised individuals, pregnant women, and those with pre-existing liver disease. Evidence also indicates transmission via blood transfusion and parenteral routes, emphasizing the need for improved surveillance and prevention (2, 3).

Data on HEV prevalence in Eastern European countries, such as the Republic of Moldova, remain sparse, despite the presence of socio-economic challenges and gaps in healthcare access that may facilitate HEV transmission (4). Certain groups face an increased risk of HEV infection because of specific vulnerabilities. Blood donors represent a critical focus due to the potential for transfusion-transmitted HEV, as asymptomatic donors with HEV viraemia pose a risk to blood safety (3). Hemodialyzed patients face an elevated risk stemming from frequent exposure to blood products, medical equipment, and their immunosuppressed status, with studies showing significantly higher HEV seroprevalence in this population (5).

Medical workers, due to occupational exposure, are at risk of HEV infection through contact with infected patients or contaminated materials (6). Tuberculosis (TB) patients may experience exacerbated liver complications if co-infected with HEV, particularly because of the hepatotoxic nature of TB treatments and their weakened immune systems (7). Intravenous drug users (IDUs) are also highly vulnerable due to unsafe injection practices, needle sharing, and behaviors that facilitate viral transmission, with studies showing higher HEV prevalence in this group compared to the general population (8).

This study aims to determine and compare the seroprevalence of hepatitis E virus (HEV) among five distinct high-risk populations in Moldova by measuring the prevalence of Anti-HEV IgG and IgM antibodies.

MATERIAL AND METHODS

This study has assessed the seroprevalence of hepatitis E virus (HEV) among five distinct high-risk populations in the Republic of Moldova: blood donors, hemodialyzed patients, medical workers, tuberculosis (TB) patients, and intravenous drug users (IDUs). This cross-sectional descriptive-epidemiological study was conducted over the 2019–2023 period, with samples collected progressively but tested at the end, enabling a reliable assessment of HEV seroprevalence.

SAMPLING AND STUDY POPULATION

Each risk group was sampled separately based on predefined stratification criteria, ensuring a representative distribution. Participants were selected through a stratified, multistage random sampling method. Selection was not based on pre-existing lists for all groups, but rather on eligibility criteria at the time of sample collection. In groups where registries were available (e.g., blood donors, hemodialyzed patients, medical workers), recruitment was facilitated through institutional databases. Stratification was performed within each group based on relevant demographic and epidemiological characteristics, such as age, sex, and geographical area.

At each stage, individuals were randomly chosen to ensure representative distribution within each group. The sample size for each at-risk population

was determined based on previously reported HEV seroprevalence rates in similar groups from various studies. The following prevalence estimates were used as reference values:

- Blood donors: Studies in Europe have reported HEV seroprevalence ranging from 4.7% to 52.5% (9), with a conservative estimate of 10% used for sample size calculation.
- Hemodialyzed patients: Seroprevalence in Bulgaria is 6.2%, with European studies generally reporting lower values (10). A reference prevalence of 5% was used.
- Medical workers: Higher HEV seroprevalence has been reported among clinical staff compared to non-clinical workers, with studies showing rates up to 23.7% among nurses (11). A prevalence estimate of 15% was applied.
- Tuberculosis (TB) patients: Limited data exist on HEV prevalence in TB patients, but studies suggest a potential link with hepatotoxicity. Based on available evidence, a 12% prevalence was used.
- Intravenous drug users (IDUs): Global reports indicate HEV seroprevalence around 6.1% and (12, 13), with 6% used as the reference value.

To determine the appropriate sample size for each high-risk population group, we used the standard formula for sample size estimation in prevalence studies:

$$n = \frac{Z^2 P(1 - P)}{d^2}$$

whereas:

n = required sample size

Z = 1.96 (Z-score for a 95% confidence level)

P = estimated prevalence for each group, based on previous studies

d = margin of error (set at 5%)

By using the formula, the following sample sizes were obtained for each high-risk group: Blood Donors – 139, Hemodialyzed Patients – 73, Medical Workers – 196, Tuberculosis (TB) Patients – 163, and Intravenous Drug Users (IDUs) – 87, resulting in a total calculated sample size of 658.

The inclusion of 1634 subjects from the five high-risk groups in the study exceeded the required calculated sample size – 658 individuals, based on a 5% margin of error, ensuring that the number of participants is statistically representative for assessing hepatitis E virus seroprevalence in these populations (tab. 1).

Table 1. Comparison of Calculated and Article Sample Sizes.

Group	Calculated Sample Size	Article Sample Size
Blood Donors	139	794
Hemodialyzed Patients	73	83
Medical Workers	196	468
TB Patients	163	201
IDUs	87	88
Total	658	1634

DATA COLLECTION AND ETHICAL CONSIDERATIONS

Samples were collected progressively over the 2019–2023 period, but all testing was conducted at the end of the study, ensuring that the results reflect a single cross-sectional analysis rather than multiple independent datasets. Seroprevalence results represent the cumulative findings from all collected samples, as all testing was performed at the end of the study. Therefore, the reported prevalence does not correspond to any specific year within the 2019–2023 period but rather reflects an overall assessment of HEV exposure across the entire timeframe. This approach allowed for a comprehensive evaluation of HEV seroprevalence while maintaining the methodological integrity of a cross-sectional study. Blood samples were collected at designated medical institutions, including hospital laboratories, dialysis centers, and TB treatment clinics across Moldova. Prior to sample collection, all participants provided written informed consent. The study was approved by the Research Ethics Committee of the National Public Health Agency (Protocol No. N2018-055, dated 24.12.2018), ensuring compliance with ethical guidelines and confidentiality standards.

LABORATORY ANALYSIS

A total of 5 mL of venous blood was collected from each participant by trained phlebotomists using standard aseptic techniques. Blood samples were stored at 2-8°C and transported within 24 hours to the National Agency for Public Health Laboratory for further analysis. Serum samples were tested for Anti-HEV IgG and IgM using ELISA kits (DIA.PRO, Milan, Italy), with: Sensitivity – 96.3%, Specificity – 98.2%. The positivity threshold was determined based on the manufacturer's optical density (OD) ratio method, where samples with an OD ratio ≥1.1 were classified as positive, <0.9 as negative, and values between 0.9-1.1 as borderline and subject to retesting. For quality control, each assay included positive and negative controls to ensure assay reliability. Additionally, 10% of the samples were retested independently for reproducibility assessment.

STATISTICAL ANALYSIS

Seroprevalence was calculated as the proportion of positive cases within each group using the following formula:

$$Seroprevalence\ (\%) = \frac{\text{Positive cases}}{\text{Total tested individuals}} \times 100$$

To estimate the precision of these proportions, 95% confidence intervals (CIs) were computed using the Wilson score method, which is more accurate than the normal approximation for small sample sizes. The CI was determined by:

$$CI = \hat{p} \pm z_{\alpha/2} \times \sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$$

where $\hat{p}$ represents the observed proportion of positive cases, $z_{\alpha/z}$ is the critical value for a 95% CI (1.96), and n is the total sample size.

For comparisons between groups, statistical significance was assessed using the Chi-square (χ^2) test, calculated as:

$$x^2 = \sum \frac{(O-E)^2}{E}$$

where O represents the observed frequency in each category and E is the expected frequency under the null hypothesis.

For comparisons involving small sample sizes (n < 5 per category), Fisher's exact test was applied to ensure statistical validity. This test is particularly useful when expected frequencies are too low for the Chi-square test to be reliable, as it calculates an exact probability rather than relying on approximations. Statistical significance was determined using a p-value threshold of 0.05, with results considered significant if $p < 0.05$, indicating a non-random association between HEV seroprevalence and the studied risk factors. Statistical analyses were performed using Epi Info 7.2 software to ensure consistency and accuracy in data interpretation.

RESULTS

Table 2 presents the seroprevalence of hepatitis E markers among the examined population groups. The analysis includes two markers – Anti-HEV IgG and Anti-HEV IgM – with the number of positive cases and their respective percentages detailed.

Table 2. Seroprevalence of hepatitis E virus markers among various risk groups in the Republic of Moldova.

Risk group	Marker					
	Anti-HEV IgG			Anti-HEV IgM		
	Total examined	Positive	% (95% CI)	Total examined	Positive	% (95% CI)
Blood donors	794	76	9.6 (7.7-11.8)	568	47	8.3 (6.3-10.8)
Hemodialysed patients	83	38	45.8 (34.8-57.1)	37	8	21.6 (9.8-38.2)
Medical workers	468	55	11.8 (9.1-15.0)	63	24	38.1(26.1-51.2)
TB patients	201	24	11.9 (7.8-17.2)	115	9	7.8 (3.6-14.3)
IDUs	88	18	20.5 (12.6-30.4)	88	0	0
Total	1634	211	12.9 (11.0-15.1)	871	88	10.1 (8.1-12.0)

Out of 794 tested blood donors, 9.6% (95% CI: 7.7-11.8) tested positive for Anti-HEV IgG, indicating past exposure to HEV. Similarly, 8.3% (95% CI: 6.3-10.8) from 568 of blood donors tested positive for Anti-HEV IgM, suggesting recent HEV infection.

The seroprevalence of HEV markers among 83 hemodialysed patients is notably higher compared to blood donors ($p<0.05$). 45.8% (95% CI: 34.8-57.1) of hemodialysed patients tested positive for Anti-HEV IgG, indicating a substantially higher rate of past exposure to HEV. Additionally, 21.6% (95% CI: 9.8-38.2) or 37 individuals of hemodialysed patients tested positive for Anti-HEV IgM, indicating a considerable proportion experiencing recent HEV infection.

Among the 468 tested medical workers, the seroprevalence of Anti-HEV IgG is 11.8% (95% CI: 9.1-15.0), this indicates a moderate level of past exposure to HEV among this group. However, the seroprevalence of Anti-HEV IgM is substantially higher at 38.1% (95% CI: 26.1-51.2).

Out of 201 tested TB patients, 11.9% (95% CI: 7.8-17.2) tested positive for Anti-HEV IgG, indicating past exposure to HEV. In contrast, only 7.8% (95% CI: 3.6-14.3) of TB patients tested positive for Anti-HEV IgM, suggesting a lower rate of recent HEV infection.

Finally, out of 88 intravenous drug users (IDUs) tested, 20.5% (95% CI: 12.6-30.4) tested positive for Anti-HEV IgG, indicating past exposure to HEV. Notably, none of the IDUs tested positive for IgM, which may reflect lower rates of recent HEV infection or underreporting caused by limited healthcare access.

Next, we will present the results of more detailed testing for each of the investigated groups. Thus, the results for the blood donors are presented in the table 3.

Table 3. Seroprevalence of HEV markers by factors among blood donors from the Republic of Moldova.

Factor	Marker					
	Anti-HEV IgG			Anti-HEV IgM		
	Total examined	Positive	% (95% CI)	Total examined	Positive	% (95% CI)
Sex						
Male	551	56	10.2 (7.9-13.0)	381	31	8.1 (5.8-11.3)
Female	243	20	8.2 (5.1-12.4)	187	16	8.6 (5.0-13.5)
Age group (years)						
≤20	44	3	6.8 (1.4-18.7)	41	3	7.3 (1.5-19.9)
21-40	434	35	8.1 (5.9-11.0)	324	19	5.9 (3.8-9.0)
41-60	309	37	12.0 (8.8-16.1)	201	25	12.4 (8.2-17.8)
≥61	7	1	14.3 (0.4-57.9)	2	0	0
Geographical zone						
North	155	16	10.3 (6.0-16.2)	77	7	9.1 (3.7-17.8)
Central	487	37	7.6 (5.6-10.3)	377	27	7.2 (5.0-10.2)
South	152	23	15.1 (9.8-21.8)	114	13	11.4 (6.2-18.7)

Among blood donors, the seroprevalence of Anti-HEV IgG was slightly higher in males (10.2%, 95% CI: 7.9–13.0) compared to females (8.2%, 95% CI: 5.1–12.4). Similarly, Anti-HEV IgM seroprevalence was 8.1% (95% CI: 5.8–11.3) in males and 8.6% (95% CI: 5.0–13.5) in females, with no statistically significant differences ($p>0.05$), indicating comparable exposure risks between sexes.

Seroprevalence rates increased with age, suggesting cumulative exposure to HEV over time. Individuals aged ≥61 years had the highest Anti-HEV IgG seroprevalence (14.3%, 95% CI: 0.4–57.9), while those aged 41–60 years exhibited the highest Anti-HEV IgM seroprevalence (12.4%, 95% CI: 8.2–17.8). In contrast, individuals aged ≤20 years had the lowest rates for Anti-HEV IgG (6.8%, 95% CI: 1.4–18.7) and Anti-HEV IgM (7.3%, 95% CI: 1.5–19.9).

Geographically, donors from the South zone had the highest Anti-HEV IgG seroprevalence (15.1%, 95% CI: 9.8–21.8), followed by the North (10.3%, 95% CI: 6.0–16.2) and Central zones (7.6%, 95% CI: 5.6–10.3). Anti-HEV IgM seroprevalence was also highest in the South (11.4%, 95% CI: 6.2–18.7), reflecting potential regional differences in HEV transmission dynamics, environmental factors, and population characteristics.

Table 4 presents the seroprevalence rates of HEV markers among hemodialysed patients from the Republic of Moldova, categorized by various factors such as sex, age group, and geographical zone.

Table 4. Seroprevalence of HEV markers by factors among hemodialysed patients from the Republic of Moldova.

Factor	Marker					
	Anti-HEV IgG			Anti-HEV IgM		
	Total examined	Positive	% (95% CI)	Total examined	Positive	% (95% CI)
Sex						
Male	46	19	41.3 (27.0-56.8)	18	6	33.3 (13.3-59.0)
Female	37	19	51.4 (34.4-68.1)	19	2	10.5 (1.3-33.1)
Age group (years)						
21-40	10	2	20.0 (2.5-55.6)	2	0	0
41-60	39	17	43.6 (27.8-60.4)	16	3	18.8 (4.0-45.6)
≥61	34	19	55.9 (37.9-72.8)	19	5	26.3 (9.1-51.2)
Geographical zone						
North	25	13	52.0 (31.3-72.2)	13	1	7.7 (0.2-36.0)
Central	25	9	36.0 (18.0-57.5)	8	3	37.5 (8.5-75.5)
South	32	15	46.9 (29.1-65.3)	15	4	26.7 (7.8-55.1)

Among hemodialyzed patients, Anti-HEV IgG seroprevalence was 41.3% (95% CI: 27.0–56.8) in males and slightly higher in females at 51.4% (95% CI: 34.4–68.1). Conversely, Anti-HEV IgM seroprevalence was higher in males (33.3%, 95% CI: 13.3–59.0) compared to females (10.5%, 95% CI: 1.3–33.1), though the differences were not statistically significant ($p>0.05$).

Patients aged ≥61 years showed the highest seroprevalence for both Anti-HEV IgG (55.9%, 95% CI: 37.9–72.8) and Anti-HEV IgM (26.3%, 95% CI: 9.1–51.2). The youngest group (21–40 years) had the lowest rates, with 20.0% (95% CI: 2.5–55.6) for IgG and no IgM positivity. Patients aged 41–60 years exhibited intermediate seroprevalence levels.

Clear geographical differences were observed, with the North zone reporting the highest Anti-HEV IgG seroprevalence (52.0%, 95%CI: 31.3–72.2), while the Central zone had the lowest (36.0%, 95%CI: 18.0–57.5). In contrast, the highest Anti-HEV IgM seroprevalence was found in the Central zone (37.5%, 95%CI: 8.5–75.5), followed by the South zone (26.7%, 95%CI: 7.8–55.1), highlighting regional variations in HEV exposure.

Furthermore, the data gathered from the testing of medical personnel are shown in Table 5.

Table 5. Seroprevalence of HEV markers by factors among medical workers from the Republic of Moldova.

Factor	Marker					
	Anti-HEV IgG			Anti-HEV IgM		
	Total examined	Positive	% (95% CI)	Total examined	Positive	% (95% CI)
Sex						
Male	57	4	7.0 (1.9-17.0)	8	3	37.5 (8.5-75.5)
Female	411	51	12.4 (9.6-15.9)	55	21	38.2 (25.4-52.3)
Age group (years)						
21-40	127	21	16.5 (10.5-24.2)	24	10	41.7 (22.1-63.4)
41-60	230	22	9.6 (6.1-14.1)	26	10	38.5 (20.2-59.4)
≥61	111	12	10.8 (5.7-18.1)	13	4	30.8 (9.1-61.4)
Geographical zone						
North	122	18	14.8 (9.0-22.3)	19	3	15.8 (3.4-39.6)
Central	179	12	6.7 (3.5-11.4)	18	3	16.7 (3.6-41.4)
South	151	20	13.2 (8.3-19.7)	20	5	25.0 (8.7-49.1)
Professional group						
Medical doctor	26	1	3.8 (0.1-19.6)	1	0	0
Nurse	59	14	23.7 (13.6-36.6)	14	3	21.4 (4.7-50.8)
Auxiliary staff	35	3	8.6 (1.8-23.1)	3	0	0

The seroprevalence rates displayed notable variation across several categories, reflecting the intricate interplay of factors influencing HEV infection among medical workers in the Republic of Moldova.

Among medical workers, Anti-HEV IgG seroprevalence was lower in males (7.0%, 95% CI: 1.9–17.0) compared to females (12.4%, 95% CI: 9.6–15.9), while Anti-HEV IgM rates were similar between males (37.5%, 95% CI: 8.5–75.5) and females (38.2%, 95% CI: 25.4–52.3). Age-related trends showed the highest seroprevalence rates in individuals aged 21–40 years for both Anti-HEV IgG (16.5%, 95% CI: 10.5–24.2) and Anti-HEV IgM (41.7%, 95% CI: 22.1–63.4), suggesting greater vulnerability due to occupational hazards. Geographically, the Central zone had the lowest Anti-HEV IgG (6.7%, 95% CI: 3.5–11.4) and Anti-HEV IgM (16.7%, 95% CI: 3.6–41.4) seroprevalence, while other regions showed higher rates, reflecting regional differences in transmission dynamics. Moreover, nurses had the highest seroprevalence of Anti-HEV IgG (23.7%, 95% CI: 13.6–36.6) and Anti-HEV IgM (21.4%, 95% CI: 4.7–50.8) among professional roles, which is likely attributed to increased occupational exposure.

Another group in the study included patients with TB, and the results of their tests are presented below (see Table 6).

Table 6. Seroprevalence of HEV markers by factors among TB patients from the Republic of Moldova.

Factor	Marker					
	Anti-HEV IgG			Anti-HEV IgM		
	Total examined	Positive	% (95% CI)	Total examined	Positive	% (95% CI)
Sex						
Male	128	18	14.1 (8.6-21.3)	93	8	8.6 (3.8-16.2)
Female	73	6	8.2 (3.1-17.0)	22	1	4.5 (0.1-22.8)
Age group (years)						
21-40	55	5	9.1 (3.0-20.0)	38	3	7.9 (1.7-21.4)
41-60	95	11	11.6 (5.9-19.8)	50	4	8.0 (2.2-19.2)
≥61	50	8	16.0 (7.2-29.1)	27	2	7.4 (0.9-24.3)

Among male TB patients, the seroprevalence of Anti-HEV IgG was 14.1% (95% CI: 8.6-21.3), while in females, it was 8.2% (95% CI: 3.1-17.0). For Anti-HEV IgM, males had a seroprevalence of 8.6% (95% CI: 3.8-16.2), and females had 4.5% (95% CI: 0.1-22.8), indicating higher rates in males ($p>0.05$).

Seroprevalence varied by age group. The ≥61 age group had the highest Anti-HEV IgG seroprevalence at 16.0% (95% CI: 7.2-29.1), followed by 41-60 years at 11.6% (95% CI: 5.9-19.8), and 21-40 years at 9.1% (95% CI: 3.0-20.0). For Anti-HEV IgM, the ≥61 group had the highest at 7.4% (95% CI: 0.9-24.3), followed by 41-60 years at 8.0% (95% CI: 2.2-19.2). These results suggest a potential link between age and HEV exposure.

Table 7 presents the results of the study regarding the testing of intravenous drug users (IDUs) for hepatitis E virus markers.

Table 7. Seroprevalence of Anti-HEV IgG marker by factors among IDUs from the Republic of Moldova.

Factor	Anti-HEV IgG		
	Total examined	Positive	% (95% CI)
Sex			
Male	46	11	23.9 (12.6-38.8)
Female	42	7	16.7 (7.0-31.4)
Age group (years)			
21-40	30	5	16.7 (5.6-34.7)
41-60	44	11	25.0 (13.2-40.3)
≥61	14	2	14.3 (1.8-42.8)

Among male IDUs, the seroprevalence of Anti-HEV IgG was 23.9% (95% CI: 12.6-38.8), and among females, it was 16.7% (95% CI: 7.0-31.4), indicating a higher prevalence in males, though not significantly different ($p>0.05$).

For age groups, the 41-60 years group had the highest seroprevalence of Anti-HEV IgG at 25.0% (95% CI: 13.2-40.3), followed by the 21-40 years group at 16.7% (95% CI: 5.6-34.7). The ≥61 years group had the lowest rate at 14.3% (95% CI: 1.8-42.8). These findings suggest a potential age-related trend in Anti-HEV IgG prevalence among IDUs, with middle-aged individuals showing higher rates.

As mentioned earlier, all IDUs tested for the acute phase marker of hepatitis E virus – Anti-HEV IgM, have tested negative.

DISCUSSION

The study established an overall seroprevalence of anti-HEV IgG at 12.9% (95% CI: 11.0-15.1) and anti-HEV IgM at 10.1% (95% CI: 8.1-12.0) among at-risk populations in the Republic of Moldova. Among blood donors, the seroprevalence of anti-HEV IgG was 9.6% (95% CI: 7.7-11.8) and anti-HEV IgM was 8.3% (95% CI: 6.3-10.8), consistent with European studies showing anti-HEV IgG rates ranging from 4.7% to 52.5% [9]. The trend of increasing seroprevalence with age aligns with other findings, such as Wong et al., where anti-HEV IgG prevalence increased from 0.6% in younger donors to 7.4% in older donors (14).

The geographical distribution of seroprevalence among blood donors revealed higher rates in the South (15.1% for anti-HEV IgG and 11.4% for anti-HEV IgM), potentially due to environmental or socio-economic factors. These regional differences align with previous studies indicating that rural areas may have a higher prevalence of HEV due to lower sanitation levels (10).

Hemodialyzed patients showed significantly higher anti-HEV IgG seroprevalence at 45.8% (95% CI: 34.8-57.1) and anti-HEV IgM at 21.6% (95% CI: 9.8-38.2). These rates exceed those reported in Bulgaria (6.2%) and Greece (10.4%) but are lower than studies in Iran showing up to 68.6% (15). The correlation between advancing age and higher seroprevalence was observed, consistent with findings from Japan and Sweden, where older patients exhibited significantly higher seroprevalence (16, 17). Gender differences in this group were minimal, though males had slightly higher anti-HEV IgM levels, potentially reflecting variations in immune response (18).

Medical workers exhibited an anti-HEV IgG seroprevalence of 11.8% (95% CI: 9.1-15.0) and anti-HEV IgM of 38.1% (95% CI: 26.1-51.2). Comparable results were reported by Lu et al., who found higher prevalence rates among clinical staff compared to non-clinical staff [19]. Interestingly, nurses demonstrated the highest anti-HEV IgG levels at 23.7% (95% CI: 13.6-36.6), likely due to frequent patient contact, while auxiliary staff also showed elevated levels (8.6%, 95% CI: 1.8-23.1) due to their roles in sanitation and cleaning (11). These findings highlight the occupational risks associated with HEV exposure.

Among TB patients, anti-HEV IgG prevalence was 11.9% (95% CI: 7.8-17.2) and anti-HEV IgM was 7.8% (95% CI: 3.6-14.3). Male patients showed higher seroprevalence than females, consistent with studies such as Sarda et al., which identified HEV as a significant factor in hepatotoxicity during TB treatment [20]. The age-related increase in seroprevalence among TB patients aligns with cumulative exposure over time and the immunosuppressive effects of TB treatment.

Intravenous drug users had an anti-HEV IgG seroprevalence of 20.5% (95% CI: 12.6-30.4), consistent with global studies reporting rates between 6.1%

and 23.0% (12, 13). Male IDUs exhibited higher seroprevalence than females (23.9% vs. 16.7%), although the difference was not statistically significant. Age-related trends indicate higher seroprevalence in middle-aged users (41-60 years), as seen in other studies (21). The absence of anti-HEV IgM among IDUs suggests either low levels of recent infections or underreporting due to limited healthcare access.

These findings emphasize the importance of targeted interventions like routine screenings, health education, and better sanitation for high-risk groups. For hemodialysis patients, it's vital to have more rigorous blood product screening and stricter hygiene practices during dialysis. Medical workers also need stronger protective measures and awareness campaigns to reduce occupational risks. For those with tuberculosis and injecting drug users, improving healthcare access and educating them about HEV transmission could help significantly lower infection rates (1).

CONCLUSIONS

1. Hepatitis E virus infection is a serious health issue among at-risk populations in the Republic of Moldova.
2. Adequate prevention and control measures must be implemented by public health authorities. Education and awareness efforts targeting vulnerable groups are essential to reduce the risk of infection.
3. Developing more efficient prevention strategies can significantly help limit the spread of the virus.
4. Implementing these measures could reduce the disease burden and improve public health outcomes.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

ETHICS APPROVAL

The study was conducted in the Laboratory of Viral Hepatitis and Bloodborne Infections at the National Agency for Public Health in the Republic of Moldova. Ethical approval was obtained from the Research Ethics Committee of the National Public Health Agency (Protocol No. N2018-055, dated 24.12.2018).

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LEVEL OF PROFESSIONAL BURNOUT AMONG FAMILY PHYSICIANS IN THE REPUBLIC OF MOLDOVA AND CERTAIN ASPECTS REGARDING ITS CONTRIBUTING FACTORS

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ABSTRACT:

Introduction Family medicine represents a key component of the healthcare system, a specialty characterized by fragmented work, high demands from patients/families/communities, and often conflicting interactions, all of which are conditions that predict stress and the onset of burnout. The aim of this study was to assess the degree to which family physicians in the Republic of Moldova are affected by professional burnout, as well as to identify its determining factors.

Materials and methods The research was conducted as a descriptive cross-sectional study from November 2023 to February 2024, on a sample of 352 family doctors.

Rezults The results show that 100% of family physicians were affected by professional burnout. The most prominent dimension of the burnout syndrome was psycho-emotional exhaustion, with a high level identified in 45.5% of respondents. Family physicians in the younger age group (36-45 years) were more affected by burnout. Family physicians working in urban areas were more affected than those in rural areas. According to the respondents, professional factors were the main contributors to the development of burnout syndrome.

Conclusions The professional burnout syndrome was identified in all family physicians involved in the study, with the dimension of psycho-emotional exhaustion being the factor with the greatest impact.

Keywords Professional burnout syndrome, burnout syndrome, family physician, primary healthcare.

NIVELUL DE ARDERE PROFESIONALĂ AL MEDICILOR DE FAMILIE DIN REPUBLICA MOLDOVA ȘI UNELE ASPECTE PRIVIND FACTORII CONTRIBUTIVI AI ACESTUIA

Introducere Medicina de familie reprezintă o verigă esențială a sistemului de sănătate, specialitate ce presupune muncă fragmentată, solicitare majoră de la pacienți/familie/comunitate, interacțiuni adesea conflictuale, condiții ce prezic stresul și apariția burnout-ului. Scopul cercetării a fost de a evalua gradul de afectare prin sindromul de ardere profesională a medicilor de familie din Republica Moldova, precum și factorii determinanți ai acestuia.

Materiale și metode Cercetarea a fost realizată având la bază un studiu de tip selectiv descriptiv, efectuat în perioada noiembrie 2023-februarie 2024, asupra unui eșantion de 352 de medici de familie.

Rezultate Rezultatele arată că sindromul de ardere profesională a afectat medicii de familie în proporție de 100%. Cea mai exprimată dimensiune a sindromului burnout a fost epuizarea psiho- emoțională, nivel înalt depistat la 45,5% dintre respondenți. Mai afectați de burnout au fost medicii de familie de vârstă tânără între 36-45 de ani. Medicii de familie din mediul urban sunt mai afectați decât cei din mediul rural. În viziunea respondenților, factorii profesionali sunt principalii care au condus la instalarea sindromului de ardere profesională.

Concluzii Sindromul arderii profesionale a fost depistat la toți medicii de familie implicați în cercetare, dimensiunea epuizare psiho-emoțională fiind factorul cu cel mai mare impact.

Cuvinte cheie Sindromul arderii profesionale, sindromul burnout, medic de familie, asistența medicală primară.

ABBREVIATIONS:

SAP	- Professional Burnout Syndrome;
AMP	- Primary Healthcare;
EGPRN	- European General Practice Research Network;
IMSP AMT	- Public Medical-Sanitary Institution Territorial Medical Association;
OMF	– Family Physician's Office;
CS	- Health Center;
CMF	- Family Physicians' Center.

INTRODUCTION

Professional burnout among family physicians is a current and important problem in the medical field globally (1).

Primary healthcare provided by the family physician together with their team represents the first point of contact between the healthcare system and the individual, ensuring non-discriminatory access and including activities such as prevention, early disease detection, counseling, curative care, and support, all aimed at meeting the health needs of the community (2). In this context, the family physician becomes responsible for managing the multitude of events that lead to a decline in the health status of the individual, the family, and society as a whole. As a consequence, the exhaustion of work resources can lead to professional burnout – a condition that causes physical, psychological, and emotional disorders, resulting from insufficient control of chronic workplace stress, and becoming a significant public health issue (3).

The topic of professional burnout was first addressed by the American psychoanalyst H.J. Freudenberger in 1974 in his work *"Staff Burn-out"* (4). In the early 1980s, it was postulated that: *"Burnout is the index of the mismatch between what people are and what they have to do; it represents the erosion of values, dignity, spirit, and will – an erosion of the human soul"*. It is a modern "disease" of the century – complex and three-dimensional – characterized by emotional exhaustion, depersonalization, and reduced personal accomplishment. It spreads rapidly like a tornado, sweeping away countless specialists and causing deep fractures in the system. *Emotional exhaustion* is the core and most commonly encountered component of professional burnout, defined by a feeling of emotional strain that leads to the complete depletion of one's emotional resources. *Depersonalization* refers to the tendency to develop negative, hostile, cold, or demeaning attitudes toward others. *Reduced personal accomplishment* is characterized by feelings of reduced productivity and a lack of confidence in one's ability to succeed at work (5).

The development of professional burnout syndrome among healthcare workers has been widely studied in recent years. It has been shown that physicians in frontline specialties, such as family medicine, are at the highest risk of developing professional burnout, as the profession involves daily communication, responsibility, overwhelming workloads, extended hours, and limited time to complete tasks (6). There is a paradox between the ideals and the reality of family physicians' work. Primary healthcare (AMP) should function as a priority within the healthcare system, aiming at prevention, health promotion, and diagnostic and curative care. In reality, however, it is driven by disease-centered actions, fragmented work, high demands from patients/families/communities, often conflicting interpersonal relationships, and low salaries. These conditions are predictors of occupational stress and the onset of burnout (7).

Primary healthcare providers are vulnerable to distress, which directly impacts their health and is often accompanied by job dissatisfaction and the intention to leave the profession. Consequently, the physician-patient relationship can become a source of conflict, and the quality of services provided declines. Ultimately, all stakeholders are affected: the patient, the institution, and the healthcare system itself (3).

Globally, the reported prevalence of burnout among family physicians is variable, with data ranging from 2.8% to 85.7%. In 2008, a European study (EGPRN) on burnout among family physicians showed that burnout is a common issue for family doctors across Europe, with high levels reported in two-thirds of the study's respondents (6). A study conducted in the Czech Republic in January–February 2023, which aimed to estimate the prevalence and asso-

ciated determinants of professional burnout among family physicians, found that 21.8% of family doctors experienced a high level of burnout across all three dimensions. The most affected dimension was reduced personal accomplishment (56.2%), followed by emotional exhaustion (50.2%) and depersonalization (40.5%) (8). A study carried out in the Republic of Moldova within IMSP AMT Râșcani during 2018–2019 showed that one in four family physicians exhibited a high level of emotional exhaustion, one in five reported a high level of depersonalization, and one in six experienced a high level of reduced personal accomplishment in their professional activity.

Despite the large number of international studies focused on professional burnout syndrome, in the Republic of Moldova the issue of professional burnout syndrome (SAP) among family physicians is not addressed in a comprehensive manner, either from the perspective of the specific manifestation profile or from the standpoint of socio-demographic data (9). This observation highlights the importance of conducting a national-level study to identify the scope and prevalence of the phenomenon, as well as the factors associated with its development.

AIM OF THE STUDY

To assess the level of professional burnout among family physicians and to explore its predictive factors.

MATERIALS AND METHODS

To achieve the stated objective, a descriptive cross-sectional study was conducted by surveying a representative sample of 352 family physicians. Considering that the population of family physicians in the Republic of Moldova is finite (the number of family physicians in 2021 was 1,656), the sample size was calculated using the formula for descriptive studies in finite populations. The calculated sample size was verified using EpiInfo for descriptive study sample estimation (parameters considered: number of family physicians – 1,656; design effect – 1.0; standard error – 5%; p = 0.5). The recalculation reduced the required number of respondents to 312, to which 10% was added to account for non-responses, establishing a final sample size of 343 family physicians. The sample size was determined to allow for the identification of weak correlations and is representative of the entire population of family physicians in the Republic of Moldova. Inclusion criteria for the study were: family physicians employed in medical-sanitary institutions in the Republic of Moldova who expressed informed consent to participate. Based on the Maslach Burnout Inventory model, a research instrument was developed in accordance with scientific standards and international study data. The questionnaire consisted of three parts: (i) the socio-demographic section, covering eight general characteristics of the sample; (ii) the second part, based on the Maslach Scale (*Burnout Inventory*), which includes 25 items structured into three dimensions (emotional exhaustion, depersonalization, and reduced personal accomplishment) and evaluates the level of professional burnout; and (iii) the final part, which includes seven questions aimed at exploring predictive and protective factors for professional burnout. The instrument was piloted and applied in a previous study conducted in 2023 in the Republic of Moldova (10). Questionnaire distribution considered institutional level, geographic distribution, and availability for participation. A total of 260 responses were collected online. Additionally, 200 printed questionnaires were distributed across various primary healthcare institutions (OMF, CS, CMF, AMT), of which 97 were returned,

with five being invalidated. Data collection took place from November 2023 to February 2024. Descriptive statistics were presented based on variable type, central tendency and variation values depending on the distribution shape for numerical variables and proportions with 95% confidence intervals for non-numerical variables. The Shapiro–Wilk test was used to assess data distribution normality. IBM SPSS was used to generate bivariate correlations, with a significance level of $p < 0.05$ applied for the chi-square test.

RESULTS

During data processing, data were disaggregated according to various analytical criteria: age, gender, work experience, work environment, type of AMP (Primary Healthcare) institution, etc.

LEVELS OF SAP (PROFESSIONAL BURNOUT SYNDROME)

According to the data obtained from the application of the Maslach Scale, 100% of surveyed family physicians reported being affected by professional burnout syndrome; the mean score obtained was 64.32 (median = 64, IQR = 18). The lowest score recorded was 36 points (the minimum score on the scale being 25 points), found in three questionnaires, while the highest score recorded was 120 points (maximum score being 125 points), according to Maslach Burnout Inventory standards. Family physicians are affected by professional burnout syndrome to varying degrees. The majority of respondents (62.8%; 95% CI 57.6–67.7) experienced a moderate level of burnout. A low level of burnout was observed in 16.2% of participants (95% CI: 12.7–20.4), while 21.0% of family physicians (95% CI: 17.1–25.6) registered a high level of professional burnout (Fig. 1).

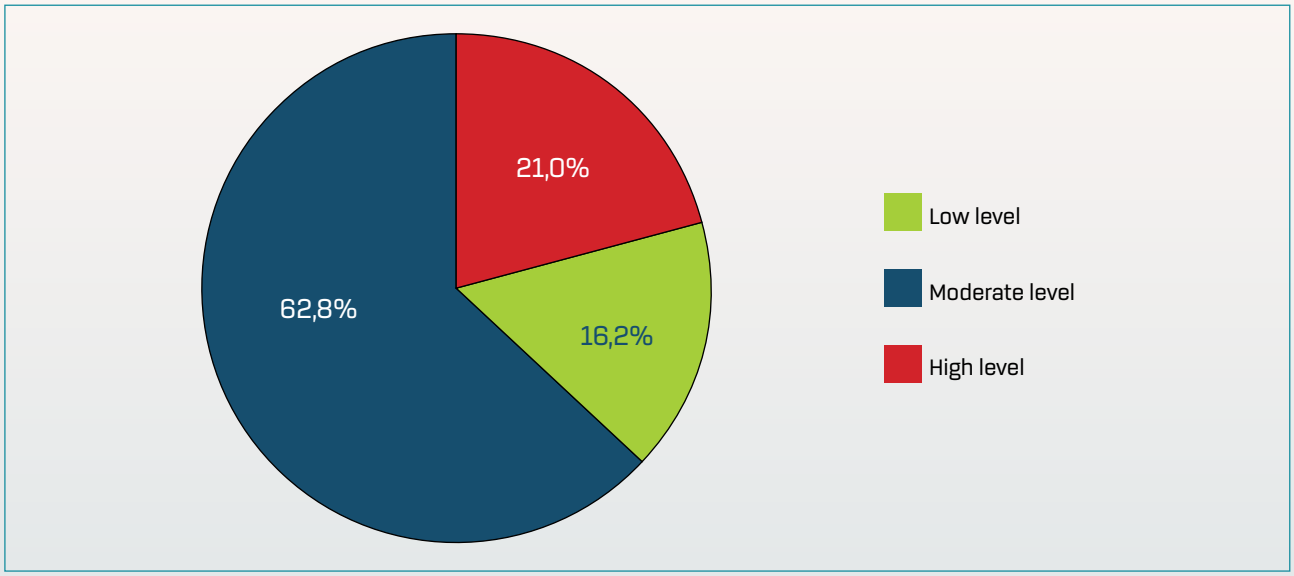

Figure 1. Levels of professional burnout among family physicians, %.

Analyzing the level of professional burnout in terms of its three dimensions – emotional exhaustion, depersonalization, and reduced personal accomplishment – we note that the dimension of SAP (Professional Burnout Syndrome) with the "highest level" of impact is psycho-emotional exhaustion. Thus, a "high" level of impact is found in 45.4% of respondents (95% CI 40.3–50.7) for psycho-emotional exhaustion, in 6.3% of respondents (95% CI 4.2–9.3) for depersonalization, and in 12.2% of respondents (95% CI 9.2–16.1) for reduced personal accomplishment (Fig. 2).

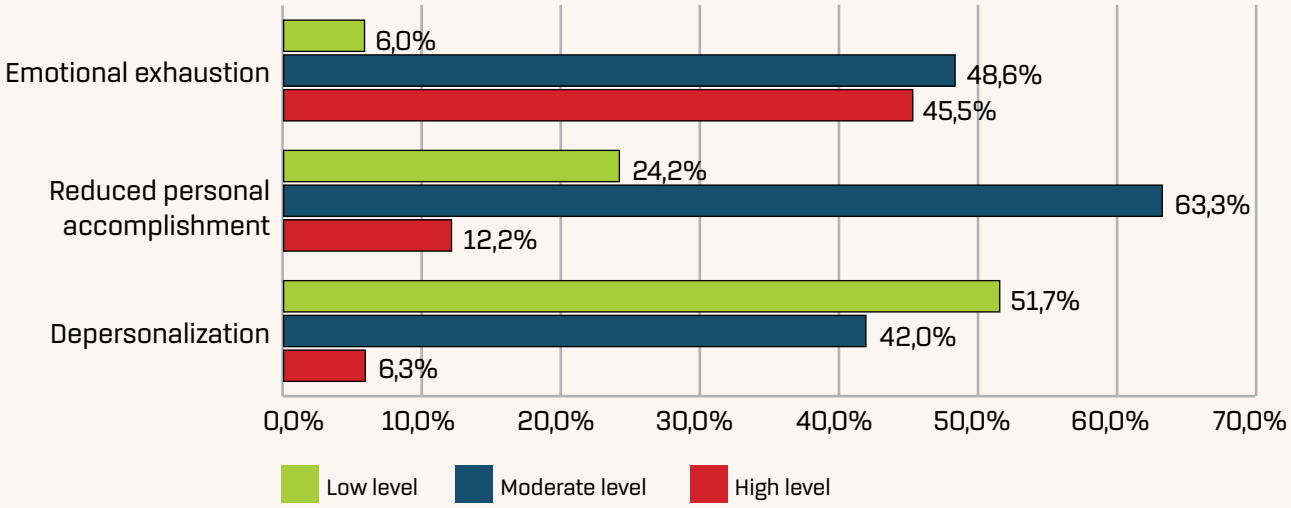

Figure 2. Levels of impact on family physicians by dimensions of professional burnout syndrome, %.

In the study, professional burnout syndrome among family physicians was analyzed in relation to age, work environment, type of institution, workload, etc. Accordingly, a high level of professional burnout was more frequently recorded (28.4%) among respondents in the 36–45 age group. The least affected by a high level of burnout were those aged 26–35 – 10.9%. At first glance, it appears that burnout levels increase with age, peaking in the 36–45 age group; however, from a statistical point of view, no significant correlation was found (t-test = 0.046, p = 0.52). Nonetheless, when analyzing the burnout dimension with the highest level of impact among family physicians – psycho-emotional exhaustion – and age, a statistically significant relationship was observed using the chi-square test ($p < 0.05$, $p = 0.02$).

Assessing the level of professional burnout according to the work environment, we find that 28.1% of physicians working in rural areas and 34.7% of those in urban areas experience a moderate level of burnout. A high level of exhaustion was reported by 7.4% of respondents from rural settings compared to 13.6% from urban areas. Analyzing the degree of impact from professional burnout syndrome by type of employing institution, we observe that a higher proportion (27.6%) of family physicians working in territorial medical associations (located in urban areas) reported a high level of burnout, whereas those working in family physician's offices showed a lower proportion of high burnout – 17.1%. About 70% of the study population work more than 35 hours per week, and these respondents are the most affected by a high level of burnout – 25.1%. Therefore, as the number of working hours increases, the level of professional burnout is also higher. Applying the chi-square test and the correlation coefficient, we found a positive correlation between these variables ($p < 0.05$; $p = 0.01$, t-test = 0.13).

PREDICTIVE FACTORS OF PROFESSIONAL BURNOUT SYNDROME IN FAMILY PHYSICIANS

The study explored the respondents' views on the determining factors that may lead to professional burnout. It is worth noting that, according to the participants' perspectives, the etiology of professional burnout syndrome is multifactorial, and the interaction between these elements contributes to the onset of the phenomenon.

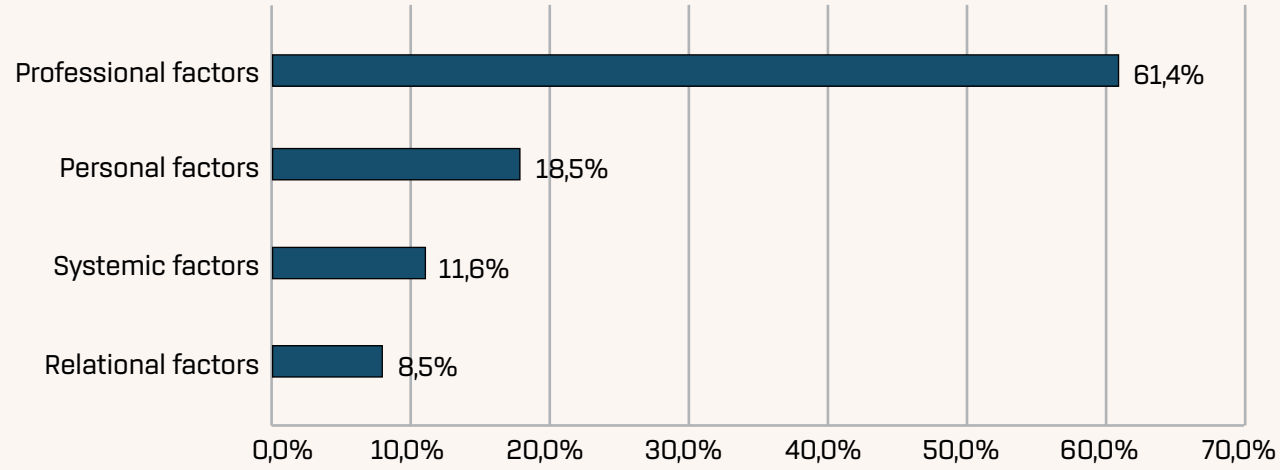

Figure 3. Factors that can lead to the development of professional burnout syndrome, %.

A significant percentage of family physicians (61.4%) consider that professional factors – such as high workload, working conditions, working overtime, lack of meal breaks, etc. – are the main contributors to exhaustion. Personal factors – such as age, lack of self-confidence, disappointment, chronic fatigue, lack of knowledge in information technology, etc. – are indicated by 18.5% of respondents. Systemic factors, including insufficient human resources, remuneration, and stress, are mentioned by 11.6% of respondents. Finally, relational factors are mentioned by the smallest proportion (8.5%), encompassing issues such as the administration's attitude towards employees, the psychosocial climate within the team, and strained relationships with patients, colleagues, superiors, etc. (Fig. 3).

Exploring family physicians' opinions on factors that could mitigate professional exhaustion reveals that the majority of respondents identified several key preventive measures. The most frequently mentioned was an adequate work schedule (74.0%), followed by support from superiors and colleagues (68.0%), sufficient human resources (67.0%), and adequate working conditions (65.0%). Support from loved ones and professional training were mentioned by 46.0% and 31.0% of respondents, respectively (Fig. 4).

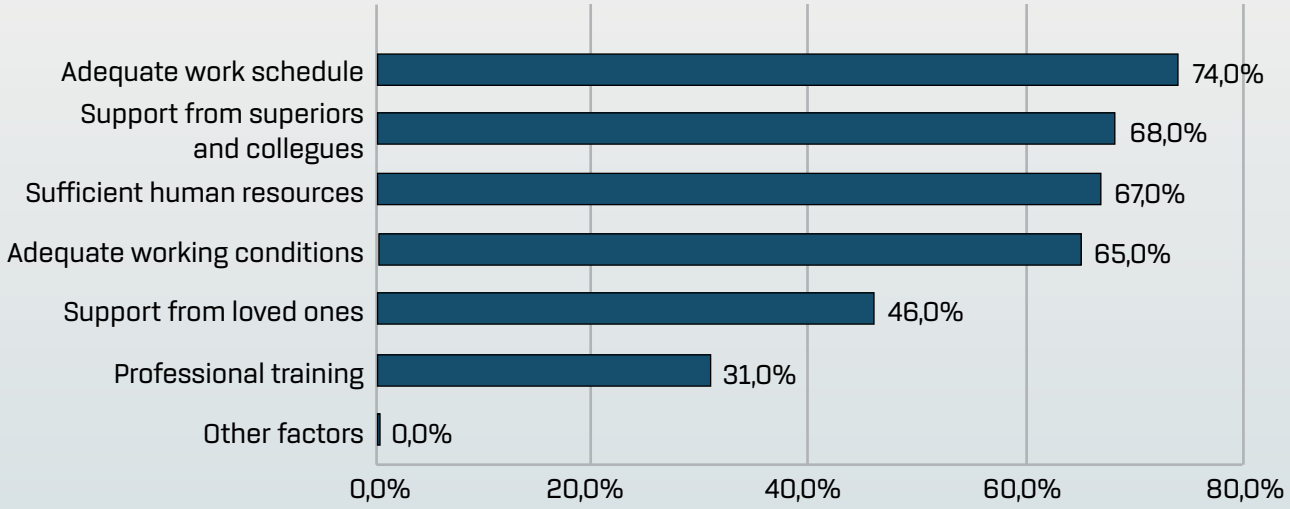

Figure 4. Factors that could mitigate professional exhaustion, %.

DISCUSSION

The results of the conducted research demonstrate that family physicians have an increased risk of being affected by professional burnout syndrome. Regarding professional burnout syndrome in family physicians, the factor with the greatest impact is emotional exhaustion, at 45.5%, which aligns with data from several international studies. A study conducted in Portugal aimed at assessing the level of professional burnout among family physicians, on a sample of 371 respondents, obtained comparable results, with the highest scores observed for the psycho-emotional exhaustion dimension (11). Another study conducted in 2023 on a sample of 127 family physicians found comparable results (3). A meta-analysis conducted by Shen et al. (2022) showed that emotional exhaustion is the dimension with the highest scores among primary care physicians (8). Therefore, it can be presumed that personnel working in primary healthcare daily face various complex tasks, influenced by diverse stressors, requiring high emotional involvement due to the specific nature of the profession.

The main risk factors for SAP (Professional Burnout Syndrome) identified in the study are: young age, an urban work environment, and workload. Comparable results have been reported by several studies conducted in recent years on primary healthcare physicians, which note the highest exposure to professional burnout syndrome among young medical professionals during their professional adaptation period (13).

According to several studies, the main triggers for professional stress and workplace exhaustion in family physicians are working conditions and high workload, unrealistic expectations for completing tasks within limited timeframes, an increasing number of patients, and insufficient human, financial, and material resources (12, 13). These factors are also considered triggers for SAP (Professional Burnout Syndrome) by a significant proportion of respondents (61.4%) in our study as well.

CONCLUSIONS

1. Professional burnout syndrome in family physicians is a widespread phenomenon, with 100% of study respondents showing signs of it. Among the three dimensions of the syndrome, *psycho-emotional exhaustion* affects a significant portion of the study population at a high level (45.5%).
2. Younger family physicians, those working in AMTs (Territorial Medical Associations – urban areas), and those with a higher workload (over 35 working hours per week) are more exposed to the risks of SAP (Professional Burnout Syndrome).
3. According to respondents' perceptions, improving working conditions, ensuring sufficient human resources, and providing social support can contribute to creating a healthy work environment, which acts as a protective factor against professional burnout syndrome.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

ETHICS APPROVAL

Ethical approval was not required by the Ethics Committee as it does not contain any ethical risks. The research consists of a survey of adults that maintains all rigor for anonymizing data and maintaining participant confidentiality.

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The article represents a synthesis of the results of the study conducted within the master's thesis defended in 2023 at the School of Public Health Management.

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ASSESSING THE EFFECTIVENESS OF THE EXTRAORDINARY TERRITORIAL PUBLIC HEALTH COMMISSIONS COORDINATION MECHANISMS IN THE COVID-19 RESPONSE IN REPUBLIC OF MOLDOVA: COORDINATION AND CAPACITY GAPS

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ABSTRACT:

Introduction The COVID-19 pandemic highlighted the need for effective coordination in managing health crises. In the Republic of Moldova, the response was managed by the National Extraordinary Public Health Commissions but implemented by the Extraordinary Territorial Public Health Commissions (TEPHCs).

Materials and methods The observational epidemiological study employed a cross-sectional design, collecting data through an online questionnaire between December 2021 and March 2022 from 294 members (94.8% response rate) of TEPHCs from 35 territorial units. The sample included 179 women (60.9%) and 115 men (39.1%). The study assessed coordination mechanisms, existing legislation, and implementation barriers.

Rezults The results show a high level of awareness of the National Response Plan to COVID-19 (92%) and recognition of its importance (95%). However, only 26% felt that the measures were clear and easy to implement. Resource issues were significant, with 65% reporting staff shortages and 75% reporting financial constraints. Despite 67% of respondents having received training, 94% expressed a need for further support in pandemic management.

Conclusions TEPHCs have been essential in managing the pandemic at local level, but their effectiveness has been hampered by an inadequate legal framework, poor communication and lack of adequate resources and training. The study recommends updating the legal framework and improving coordination mechanisms. Additional investments in preparedness are vital.

Keywords COVID-19, coordination mechanisms, public health, public safety, measures.

EVALUAREA EFICACITĂȚII MECANISMELOR DE COORDONARE A COMISIEI EXTRAORDINARE TERITORIALE DE SĂNĂTATE PUBLICĂ ÎN RĂSPUNSUL LA COVID-19: DOVEZI DIN REPUBLICA MOLDOVA

Introducere Pandemia COVID-19 a evidențiat necesitatea unei coordonări eficiente în gestionarea crizelor sanitare. În Republica Moldova, răspunsul a fost gestionat de către Comisia Națională Extraordinară de Sănătate Publică, dar implementarea a fost realizată de Comisiile Teritoriale Extraordinare de Sănătate Publică (CTESP). Primul caz COVID-19 în Moldova a fost înregistrat pe 7 martie 2020, ceea ce a dus la activarea Comisiei Naționale Extraordinare de Sănătate Publică și, ulterior, a CTESP. La 17 martie 2020 Parlamentul a declarat stare de urgență pe întreg teritoriul țării, marcând prima astfel de declarație din istoria Republicii Moldova.

Materiale și metode În studiul epidemiologic observațional, de tip transversal, s-a utilizat un chestionar online aplicat în perioada decembrie 2021 – martie 2022. Au participat 294 de membri ai CTESP (rata de răspuns: 94,8%) din 35 de unități teritoriale. Eșantionul a fost format din 179 femei (60,9%) și 115 bărbați (39,1%). Studiul a evaluat mecanismele de coordonare, cadrul legislativ și barierele de punere în aplicare.

Rezultate Studiul aplicat a arătat că 92% dintre respondenți cunoșteau despre Planul național de răspuns la COVID-19, iar 95% i-au recunoscut importanța. Cu toate acestea, doar 26% au considerat măsurile clare și ușor de aplicat. Problemele legate de resurse au fost semnificative: 65% au raportat lipsa de personal, iar 75% constrângeri financiare. Deși 67% au beneficiat de instruiri, 94% au menționat necesitatea unui sprijin suplimentar.

Concluzii CTESP au fost esențiale în gestionarea pandemiei la nivel local, dar eficiența acestora a fost afectată de cadrul legal insuficient, comunicarea deficitară, lipsa resurselor și a formării adecvate. Studiul recomandă actualizarea legislației și îmbunătățirea mecanismelor de coordonare. Investițiile în pregătire sunt esențiale.

Cuvinte cheie COVID-19, mecanisme de coordonare, sănătate publică, siguranță publică, măsuri.

INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) continues to pose a persistent global threat, with new mutations of the viral agent (SARS-CoV-2) causing ongoing socioeconomic challenges and keeping many countries in a continuous state of alert (1).

Prior to the COVID-19 pandemic, the Republic of Moldova had established a public health emergency framework based on its experiences with previous outbreaks and health crises. The Territorial Extraordinary Public Health Commissions (TEPHCs) were originally designed as local response bodies to manage regional health emergencies, including seasonal influenza outbreaks and localized infectious disease incidents. These commissions operated under the legal framework provided by Law No. 10/2009 on state supervision of public health, which defined their structure, responsibilities, and coordination mechanisms. However, prior to COVID-19, these bodies had never been activated simultaneously across the entire country for a prolonged period – an unprecedented situation that challenged their functionality and coordination capabilities.

Research question and hypothesis: This study explores how effectively the Territorial Extraordinary Public Health Commissions functioned as coordination mechanisms during the COVID-19 pandemic in the Republic of Moldova. The underlying hypothesis is that, although these commissions were essential to the pandemic response, their effectiveness was limited by structural, resource, and coordination barriers that could be identified and addressed through systematic evaluation.

The COVID-19 crisis underscores the fundamental need for a coordinated response to emergencies and their aftermath. It highlights the risks associated with uncoordinated and overly bureaucratic approaches to crisis management – regardless of whether a country is federal or unitary, centralized or decentralized. Coordination is equally essential across and among levels of government, as well as between government and non-government actors, including citizens (2).

The effectiveness of short-, medium-, and long-term responses to the coronavirus largely depends on well-structured coordination mechanisms. Government actors must align priorities, implement joint responses, support one another, and facilitate information sharing, including with citizens (3).

A crisis situation requires a rapid response to prevent escalation and mitigate damage. Adapting to uncertainty, adjusting strategies as needed, and maintaining flexibility are key elements of effective crisis management. Because emergencies have an immediate local impact, regional and local governments must have the authority to act quickly, efficiently, and responsibly.

According to the International Health Regulations, each country must ensure transparent role distribution and effective coordination mechanisms across the health sector, government, and intersectoral levels – before, during, and after public health emergencies (4).

Governance for health requires a synergistic set of policies, many of which reside in sectors other than health and outside government, and must be supported by structures and mechanisms that facilitate collaboration (5).

At the national level, the government is typically responsible for leading overall coordination in risk management (6). Effective coordination should be based on established public health emergency protocols, preparedness strategies, and response plans, including those developed for pandemic influenza (7). A critical step is to activate existing National Emergency Response Com-

mittees/Commissions to take the lead in coordinating these functions and to ensure that all partners and sectors, including international partners, are involved in response operations.

On 7 March, the World Health Organization recommended that coordination mechanisms be activated as early as possible – ideally before large-scale community transmission occurs. Existing national preparedness plans and public health incident management systems were proposed to be revised to include a joint approach involving government and the whole of society (8).

In the Republic of Moldova, the first case of COVID-19 was registered on March 7, 2020. Over 598,000 positive cases of SARS-CoV-2 and more than 11,000 deaths have been reported by the National Agency for Public Health (9).

To mitigate the impact of the COVID-19 pandemic, the Government of the Republic of Moldova established the National Extraordinary Public Health Commission and implemented a range of quarantine measures, each with a corresponding level of rigidity – from keeping only essential businesses open to allowing all facilities to operate at full capacity.

Aim. This study aims to evaluate the functionality and coordination mechanisms of the Territorial Extraordinary Public Health Commissions (TEPHCs), which serve as local public health bodies in the Republic of Moldova, during the COVID-19 pandemic. Specifically, the study seeks to:

Assess the roles, responsibilities, and effectiveness of Territorial Extraordinary Public Health Commissions in managing public health emergencies.

Identify gaps and challenges in implementing public health measures, including coordination between national and local levels, resource allocation, and stakeholder engagement.

Provide evidence-based recommendations to strengthen governance and preparedness for future public health emergencies. These recommendations, by highlighting best practices and areas for improvement in Moldova's response framework, offer a hopeful and optimistic outlook for the future. This study aims to evaluate the functionality and coordination mechanisms of the Territorial Extraordinary Public Health Commissions in the Republic of Moldova during the COVID-19 pandemic by assessing their roles, responsibilities and effectiveness; identifying critical gaps in multi-level coordination, resource allocation and stakeholder engagement; and deriving evidence-based recommendations to improve public health governance and preparedness for future emergencies. By addressing these objectives, the study directly engages with the global discourse on enhancing public health leadership and governance in times of crisis, fostering a sense of connection and relevance among the audience.

Governments worldwide are currently selecting appropriate intervention strategies to address the effects of the COVID-19 pandemic. This is a highly challenging task, as strict measures may lead to economic collapse, while a more lenient approach could result in a high death toll (10).

Many governments at all levels have reacted quickly. A combination of national and subnational measures contributes to an effective response to the COVID-19 public health and economic crisis. Leadership and coordination by the national government are critical.

The biggest challenge facing national and local governments in addressing the outbreak is to effectively coordinate actors, resources, and activities flexibly in order to design and adopt an adequate response.

The global COVID-19 pandemic of 2020–2021 required politicians to collaborate with and rely on scientists more closely than any other event in recent history (11).

Federal countries face distinctive coordination challenges. Elected regional governments, often representing various parties, can have different priorities and ideas, might not appreciate coordination, and might compete for resources and blame other governments for apparent problems (12).

This article analyzes national strategies to combat the COVID-19 pandemic in the Republic of Moldova.

In the Republic of Moldova, to ensure an adequate level of preparedness for public health emergencies, and in accordance with Article 55 of Law No. 10/2009 on state supervision of public health, the Government established the National Extraordinary Public Health Commission, and the local public administration authorities established Territorial Extraordinary Public Health Commissions (13).

The Commission's duties include preventing and managing public health emergencies through an integrated approach to all public health hazards. This involves activities related to prevention, emergency management, and multisectoral mobilization to ensure an appropriate level of preparedness for public health emergencies at the national and territorial levels. The Commission is responsible for coordinating the efforts of the central and local public administration authorities to implement measures aimed at preventing and mitigating the consequences of public health emergencies. Its responsibilities also include analyzing data received regarding the resulting situation and adopting decisions on urgent measures and subsequent actions for protecting the population and territory, including locating and addressing the consequences of such emergencies.

The presidents of the Territorial Extraordinary Public Health Commissions are the mayors or vice-mayors of the municipalities or cities. Members include representatives from key local institutions and sectors, such as those from the health sector, the education sector, the Ministry of Internal Affairs, the General Inspectorate for Exceptional Situations, and others.

This study examines the effectiveness of the Territorial Extraordinary Public Health Commissions in implementing COVID-19 response measures. The findings will help develop recommendations for improving coordination during public health emergencies.

MATERIALS AND METHODS

SAMPLE AND RESEARCH SETTING

The study was conducted using a comprehensive survey approach, targeting all members of the Territorial Extraordinary Public Health Commissions in the Republic of Moldova. The questionnaire was distributed to all commission members across the country, aiming to ensure full representation of the perspectives and experiences of individuals involved in managing public health emergencies at the territorial level. This inclusive approach allowed for a thorough and robust analysis of the functioning and coordination mechanisms of the Territorial Extraordinary Public Health Commissions during the COVID-19 pandemic.

The sampling strategy employed a comprehensive approach, targeting all 310 members of the Territorial Extraordinary Public Health Commissions across the Republic of Moldova. Of these, 294 members (94.8%) responded to the survey, representing 35 territorial administrative units.

Standardized questionnaires developed by international bodies were used and analyzed. The primary research tool was the WHO's standardized Intra-Action Review (IAR) questionnaire, which was adapted to the national context and self-administered online. Elements from the UN 2008 "Capacity Assessment Framework" model were also incorporated.

The research adopted a comprehensive quantitative approach, using a structured questionnaire designed to capture both demographic information and substantive insights related to the COVID-19 response. The statistical component of the questionnaire included questions on personal data such as date of birth, place of residence, and level of education. In addition, the questionnaire addressed several key thematic areas: coordination of the COVID-19 response, existing legislation, the declaration of the state of emergency, coordination mechanisms under Moldovan legislation, the roles and responsibilities of the Territorial Extraordinary Public Health Commissions, and related barriers and challenges.

Coordination of the COVID-19 response: The study assessed the effectiveness of coordination mechanisms at national and local levels.

Existing legislation: The study reviewed the legal framework for public health emergencies in the Republic of Moldova.

Emergency declaration: The study explored respondents' perspectives on the process and impact of declaring a state of emergency.

Coordination mechanisms under Moldovan legislation: The study examined how national legislation implements the established coordination mechanisms.

Roles and responsibilities of the Territorial Extraordinary Public Health Commissions: These commissions, established under Moldovan legislation, are responsible for coordinating and implementing public health measures at the local level. The study assessed the clarity and implementation of their mandates. Barriers and challenges: The study identified key barriers to implementing public health interventions, including issues related to resource allocation and communication.

This design enabled the collection of measurable data to analyze the effectiveness of coordination and operational strategies during the COVID-19 pandemic. The study's conclusions, supported by statistically robust evidence, hold significant relevance for the field of public health and the continued response to the pandemic.

DATA ANALYSIS PROCEDURE

Data collection was conducted between December 2021 and March 2022. The quantitative analysis of the collected data involved coding and processing using Microsoft Excel 2013, with variables such as gender, age, length of employment, and the institution represented in the Territorial Extraordinary Public Health Commissions, among others.

The study employed both quantitative and qualitative analysis techniques to process and interpret the data collected. Descriptive statistics, including fre-

quencies and percentages, were used to summarize the socio-demographic characteristics of participants and their responses to closed-ended questions. Cross-tabulation was applied to explore relationships between variables such as professional experience, educational background, and perceptions of the COVID-19 response. In addition, thematic content analysis was conducted on open-ended responses to identify common challenges and best practices.

The study involved 294 respondents, all of whom were voting members of the Territorial Extraordinary Public Health Commissions Among them:

- 179 (60.9%) were women.
- 115 (39.1%) were men.

Respective questions and performed thematic content analysis aimed to identify common (between territories) and cross-cutting (across the response pillars) themes on best practices, challenges, and priority actions.

During data analysis, the hypotheses regarding the obtained results were either confirmed or disproved. Participation in the study was voluntary and unpaid. The research concluded with proposals for developing and updating the national normative framework, as well as enhancing existing coordination mechanisms for public health emergencies in the Republic of Moldova.

RESULTS

Two hundred ninety-four questionnaires were collected from members across 35 territorial administrative units, out of a total of 310 targeted members of the Territorial Extraordinary Public Health Commissions.

In the Republic of Moldova, the coordination of responses to public health emergencies, including the COVID-19 pandemic, follows a generic approach applicable to all public health risks. Intersectoral coordination during the COVID-19 crisis was ensured by the Extraordinary Public Health Commissions at both national and local levels. Following the confirmation of the first COVID-19 case in the Republic of Moldova, the National Agency for Public Health developed a comprehensive COVID-19 preparedness and response plan. This plan was subsequently approved by the National Extraordinary Public Health Commission, which defined multisectoral objectives to protect the population during the pandemic.

The effectiveness of this approach is reflected in the responses of the members of the Territorial Extraordinary Public Health Commissions: 92% of members were aware of the COVID-19 response plan, and 95% recognized its importance. However, only 26% felt that the actions outlined in the plan were clear and easy to implement.

Multi-sectoral mobilization is essential to ensure a unified approach to managing public health emergencies. Clearly defining and regularly updating the roles and responsibilities of TEPHCs members is critical to prevent overlaps or gaps in coordination. **Results:** While 82% of respondents reported that roles were established, 58% felt they lacked sufficient knowledge and skills to effectively implement measures. This highlights gaps in professional training and capacity-building efforts.

Although coordination between national and local levels is crucial, the Territorial Extraordinary Public Health Commissions still depend heavily on the National Commission. This suggests that the decentralization process remains incomplete. **Results:** Only 56% of respondents appreciated the support from the National Commission, and just 38% felt their input was considered.

This points to a need for stronger communication and feedback mechanisms between the two levels of governance. Indicators are foundational for adjusting measures based on the alert level in each territory, but implementation remains a challenge. **Results:** Although 93% of respondents appreciated the support of public health specialists, only 58% successfully implemented the prescribed measures. This suggests operational barriers, possibly related to limited resources or insufficient training.

The absence of clear accountability mechanisms and tools for evaluating decisions reduces the efficiency and effectiveness of Territorial Extraordinary Public Health Commissions' operations. **Results:** Addressing these gaps by introducing robust monitoring frameworks can enhance transparency and ensure adherence to decisions.

Continuous training is essential to improve the ability of Territorial Extraordinary Public Health Commission members to manage public health emergencies. **Results:** Despite 67% of respondents having received training, 94% expressed a need for further support in pandemic management at the local level, underscoring a gap in practical, hands-on expertise.

Effective pandemic management requires more than plans and legislation; adequate human and financial resources are indispensable for implementation. **Results:** 65% of respondents highlighted the insufficiency of human resources, and 75% emphasized gaps in financial resources. This indicates a misalignment between strategic planning and the capacity for execution.

Local leaders play a critical role in coordinating measures, and their active involvement is key to the success of interventions. **Results:** Recognition by 80% of respondents for district presidents and healthcare representatives highlights the importance of these actors in driving local-level response efforts.

DISCUSSION

This study provides a comprehensive evaluation of the Territorial Extraordinary Public Health Commissions in Moldova during the COVID-19 pandemic, analyzing their coordination mechanisms, level of preparedness, and operational barriers. The findings are contextualized within global experiences, highlighting both shared patterns and unique challenges.

Based on the national code red alert regarding the unfavorable epidemiological situation caused by COVID-19, and at the proposal of the Government, the Parliament declared a State of Emergency throughout the territory of the Republic of Moldova from March 17 to May 15, 2020. The provisions of the Commission for Exceptional Situations of the Republic of Moldova are binding and enforceable for the heads of central and local public administration authorities, economic agents, public institutions, as well as for citizens and all other persons located within the territory of the Republic of Moldova. For the first time in the country's history, a state of emergency was declared (14).

During the state of emergency, the coordination mechanism was the Emergency Situations Commission, which issued 30 provisions. It established quarantine regimes for localities with outbreaks of infection, approved several exemptions from existing legislation, introduced restrictions for natural persons and economic agents, set rules for public procurement, and authorized charter flights or passenger transport for the repatriation of Moldovan citizens (15).

The results demonstrated that while most members of the Territorial Extraordinary Public Health Commissions (95.9%) were aware of coordina-

tion mechanisms, only 53% correctly identified the National Extraordinary Public Health Commission (CNESP) as the central coordinating body. This finding indicates gaps in communication and understanding of governance roles, which could undermine the effective implementation of public health measures.

Awareness of the Preparedness and Response Plan was high (92%), and its importance was acknowledged by 95.6% of respondents. However, only 58% reported effective implementation of measures, reflecting significant barriers such as insufficient resources, unclear legal frameworks (noted by 31.3% of respondents), and inadequate training. These challenges hinder the uniform application of public health measures across administrative levels.

Additionally, multisectoral involvement was deemed crucial but remained uneven, with 54% of respondents affirming sectoral integration, while 30% reported insufficient engagement. This discrepancy highlights the need for improved coordination across non-health sectors, which play a vital role in pandemic response efforts.

The findings align with global research that emphasizes the importance of robust coordination mechanisms, clear governance structures, and adequate resource allocation. For example:

Studies from European countries have similarly highlighted challenges in integrating multisectoral approaches during the early stages of the pandemic.

The first wave of the pandemic brought about a marked trend toward centralization within governments almost everywhere (see Table 1). As Table 1 indicates, during the spring and summer of 2020, most European countries adopted centralized strategies to manage the crisis. This approach, characterized by swift, top-down directives issued through interministerial committees, national security councils, or similar bodies, proved effective in coordinating the initial response. Heads of government were incentivized to take charge, demonstrating leadership and avoiding blame for inaction – actions that reassured both the public and policymakers.

Moldova followed a similar pattern. Shortly after the first confirmed COVID-19 case, national authorities activated the National Extraordinary Public Health Commission. A state of emergency was declared, and the Commission for Exceptional Situations became a central node for enacting measures. This shift reflected the broader European trend of governments centralizing authority to respond rapidly and decisively.

However, Moldova's administrative framework relies on Territorial Extraordinary Public Health Commissions (TEPHCs) at the local level. These commissions are legally mandated to coordinate response activities within their respective territories. Like other decentralized systems – such as Germany – Moldova faced challenges in maintaining effective horizontal and vertical coordination as the pandemic progressed. The difficulties encountered by these local commissions, despite having clearly defined responsibilities on paper and a legal mandate, often stemmed from their heavy reliance on central directives. This mirrored Germany's struggle to maintain voluntary coordination among its Länder and elicited empathy from observers for the challenges faced at the local level.

Vertical Coordination: In the Republic of Moldova, TEPHCs reported limited feedback loops with the national commission – an issue akin to the communication gaps observed between federal and regional governments in countries like Germany and Spain.

Horizontal Coordination: Despite the legal framework for multisectoral collaboration – including sectors such as health, education, and law enforcement – local commissions in Moldova reported barriers to consistent implementation. These challenges were partly due to uneven resource distribution and unclear lines of authority.

Table 1 also shows that some European countries shifted their governance approach in autumn and winter by either reasserting central authority or experimenting with forms of decentralization. Moldova similarly oscillated between strong central directives (e.g., national-level restrictions) and sporadic empowerment of local bodies. This empowerment often took the form of allowing TEPHCs to make decisions on specific local measures, such as enforcing curfews or closing non-essential businesses. Yet, as in many countries, sustaining genuine decentralization proved challenging: local actors often faced insufficient resources, while national authorities remained cautious about ceding control during a high-stakes public health crisis (1).

Early Centralization: Moldova's immediate reliance on central bodies – namely, the National Commission and the Commission for Exceptional Situations – mirrored the Europe-wide trend of consolidating power to manage the initial surge of the pandemic.

Persistent Coordination Barriers: Like decentralized systems elsewhere, Moldova's local commissions faced challenges in maintaining effective, long-term coordination with the central level, particularly evident in communication gaps and uneven resource allocation.

The case of the Republic of Moldova underscores a broader European finding: while swift centralization can be effective for immediate crisis response, durable collaboration mechanisms, clear legal frameworks, and strong local capacities are not just beneficial, but essential for long-term pandemic management. This emphasis on robust structures highlights the critical need for well-defined legal frameworks, encouraging the audience to recognize their foundational role in effective crisis governance.

The Republic of Moldova's experience aligns with the centralization–decentralization pattern observed across Europe. Early in the crisis, central governments took the reins to provide a unified response. Over time, however, sustaining collaborative, multisectoral approaches proved challenging – particularly in administrative systems like Moldova's, which depend on both strong national-level leadership and empowered local bodies.

Table 1: Centralization and decentralization by country and domain of intervention. *Eurohealth*, No. 1, 2021.

Domain of intervention		Centralisation within government (spring/summer)	Centralisation between governments (spring/summer)	Centralisation within government (autumn/winter)	Centralisation between governments (autumn/winter)	Decentralisation (any kind) (autumn/winter)
Governance	Interministerial committee, Coordination agency, National security council					
	Expert/Vaccine committee				–	–
	State of emergency/ Emergency Laws				–	–
	Centralised governance of the health care system	–		–		–

Comparisons with Taiwan and New Zealand underscore the value of clear leadership and consistent public communication, which Moldova could emulate in future preparedness efforts.

The experiences of Taiwan and New Zealand provide valuable lessons that could be adapted to the Moldovan context, despite differences in health infrastructure and political systems:

Taiwan's success factors included: 1) early activation of a central epidemic command centre that unified decision-making; 2) transparent communication through daily briefings; 3) technological integration for contact tracing and resource allocation; and 4) clear delineation of responsibilities between central and local authorities.

New Zealand implemented: 1) a four-tier alert system with clearly defined triggers and actions; 2) consistent messaging from both political and public health leadership; 3) science-based decision-making with transparent rationale; and 4) localized implementation of national guidance, accompanied by appropriate resources.

These approaches could be adapted to Moldova by:

1. Strengthening the authority and autonomy of TEPHCs, while maintaining alignment with the national strategy through improved communication channels and feedback mechanisms.

2. Implementing a transparent alert system with clear criteria for transitions between levels, accompanied by predefined resource allocation plans.
3. Developing a crisis communication framework tailored to the Moldovan media landscape and the challenges of public trust.
4. Building capacity for data-driven decision-making at local level, supported by simplified reporting systems to reduce administrative burden.
5. Establishing formal mechanisms for knowledge sharing between territorial units to facilitate peer learning.

These adaptations acknowledge Moldova's unique health infrastructure challenges, including rural-urban disparities in access to health care, a limited public health workforce, and funding constraints. They also recognize Moldova's semi-centralized governance structure, which differs from both Taiwan's unified model and New Zealand's decentralized system with strong central coordination.

While many countries reported resource constraints, Moldova's reliance on centralized decision-making mechanisms revealed specific limitations in empowering local commissions. Strengthening local autonomy, while maintaining national oversight, could help address these gaps.

The research question focused on evaluating the functionality and coordination mechanisms of the Territorial Extraordinary Public Health Commissions. The findings are significant in identifying systemic barriers – such as insufficient human (65%) and financial resources (75%), a lack of accountability mechanisms, and gaps in training – that hinder effective public health responses. Addressing these barriers through policy reforms and capacity-building initiatives could significantly enhance emergency preparedness and response.

The study also highlights the critical role of local leadership, with 80% of respondents emphasizing the importance of district presidents and healthcare representatives in driving coordinated efforts. This finding underscores the need to invest in local leadership development and strengthen intersectoral collaboration.

The study provides actionable insights for strengthening Moldova's public health governance:

Develop and implement targeted training programs for members of the Territorial Extraordinary Public Health Commissions, with a focus on pandemic management and crisis communication.

Enhance the clarity and accessibility of legal frameworks governing public health emergencies.

Allocate dedicated resources to support both central and local-level commissions, ensuring equitable distribution.

Throughout the pandemic, political leaders and policymakers took into account the views of public health specialists and the scientific community, calling for evidence-based decisions to approve and implement response measures. Countries that effectively managed the coordination of their public health specialists were best able to quickly and effectively design and implement responses that reduced the spread of infection and minimized the impact on citizens' lives and the economy.

The impact of the COVID-19 crisis is primarily perceived as a national issue, with the central government playing a critical role due to the need for a whole-of-government approach, legislative and executive authority, suffi-

cient resources, and high-level expertise. However, the local level is equally essential for several reasons. The impact of the pandemic has a significant territorial dimension, carrying important policy implications for managing its consequences. Knowledge of local conditions, culture, and institutions, as well as awareness of vulnerable segments of the population, is crucial for effective crisis management (17).

The COVID-19 pandemic revealed serious shortcomings in preparedness for and response to health emergencies at both national and global levels. Traditional health governance mechanisms were confronted with an unprecedented need to coordinate the complex and interdependent aspects of society and systems in order to manage the response (6).

COVID-19 has highlighted the need for functional governance frameworks for health emergencies. Routine governance structures must become more agile and adaptable to keep pace with the speed required for urgent and coordinated action in complex and large-scale responses. The WHO Emergency Response Framework has been instrumental in enhancing the organization's response capacity in the European Region, providing accountability, responsibility, delegation of authority, and rapid access to response resources, demonstrating significant progress in regional response capabilities.

As revealed by the COVID-19 pandemic, the existing broader governance and accountability frameworks for emergencies at both international and national levels were found to be inadequate.

Health governance and coordination mechanisms have faced an unprecedented need to interconnect various complex aspects of society with public health emergency response management systems. Studies on intergovernmental relations generally suggest that transparency in decision-making, clear communication and coordination between officials and ministers, and the use of evidence-based data enable effective collaboration and alignment, even in countries where intergovernmental relations are typically marked by high levels of conflict.

It is also suggested that aligning powers and responsibilities leads to more effective outcomes. Countries with strong public health leadership were better able to design and implement rapid and effective responses. These efforts helped reduce the spread of infection, minimize the impact on lives and the economy, and – importantly – foster a sense of connection through public engagement, making people feel involved and part of the solution. This multidisciplinary approach must be supported and embedded in policies, laws, and procedures that enable a swift response to emergency situations. It should also be continuously strengthened in line with evolving evidence, technology, skills, and the competencies required in the public health workforce. Yet to this day, many countries, both rich and poor, have not adequately invested in the systems necessary for effective response and preparedness.

The ability of decision-makers to make high-quality, timely, evidence-based, and contextually relevant decisions requires an effective command-control-coordination architecture anchored in human rights, ethics, and integrity. Such systems must be transparent, accountable, participatory, and subject to continuous monitoring to ensure their effectiveness.

An effective global health governance framework, centered on people and integrated across all levels of society, can serve as a foundation for building resilience. It must recognize the interconnected nature of risks and embrace the holistic *One Health* approach, ensuring inclusivity for all. Only through comprehensive coordination and the establishment of equitable governance structures can the world become more resilient and better prepared for future challenges – leaving no one behind.

CONCLUSIONS

Based on the analysis of the study's data, the following conclusions have been established:

1. The Territorial Extraordinary Public Health Commissions represent essential element in the management of the COVID-19 pandemic, particularly in coordinating public health measures at the local level. Their attributions and responsibilities are aligned with those of the National Extraordinary Public Health Commission.
2. The current regulatory framework governing coordination mechanisms for public health emergency preparedness is insufficient and requires significant improvement.
3. The existence of a COVID-19 prevention and response plan, along with the provision of indicators and support in the development of public health measures by the National Agency for Public Health (NAPH), contributed to improved management at the local level.
4. Communication and coordination remain weak, both horizontally (between representatives of different territorial structures) and vertically (with relevant national authorities, such as the Ministry of Health and NAPH).
5. The members of the Territorial Extraordinary Public Health Commissions require methodical support in developing action plans, setting criteria and indicators for evidence-based decision-making, and establishing control mechanisms to monitor the implementation of public health measures.
6. The members of the Territorial Extraordinary Public Health Commissions lack sufficient knowledge and skills for managing public health emergencies, including the COVID-19 pandemic, at the local level.

The COVID-19 pandemic has exposed significant deficiencies in public health emergency preparedness and response at both the national and local levels.

RECOMMENDATIONS:

1. Improve coordination and monitoring mechanisms for responding to public health emergencies, including COVID-19, at both the national and local levels;
2. Approve operating regulations for coordination mechanisms to ensure accountability of members of the Territorial Extraordinary Public Health Commissions in decision-making and implementation;
3. Update the legislative framework related to the prevention and management of public health emergencies;
4. Revise public health emergency response plans to reflect the current epidemiological situation, new scientific evidence, and lessons learned from the COVID-19 pandemic, providing members of the Commissions with an updated strategic and operational framework;
5. Develop legal provisions to regulate communication and collaboration among Territorial Extraordinary Public Health Commissions, including the establishment of formal dialogue mechanisms both horizontally (local partnerships) and vertically (with relevant authorities such as NPHA, Ministry of Health, and the Government).

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CASE PRESENTATIONS – PRÉSENTATIONS DE CAS

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CLINICAL MANAGEMENT AND OUTCOMES OF SNAKE ENVENOMATION: A CASE SERIES

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ABSTRACT

Introduction In tropical rural communities, snakebite envenomation is among the main causes of morbidity and mortality. It results in shock, hemorrhage, tissue necrosis, and swelling. Diagnosing and identifying snake species is challenging, necessitating thorough clinical assessments and point-of-care tests. Hence this case series examines follow up on the course of clinical care and management of snake envenomation cases in Erode District, India, a location known for poisonous snakes such as the spectacled cobra *(Naja naja)*, Russell's viper *(Daboia russelii)*, and common krait *(Bungarus caeruleus)*.

Materials and methods This case series summarizes the hospital experience of patients with snake envenomation who were hospitalized to a local government medical college and hospital.

Rezults Five patients were confirmed or suspected of having been envenomated by a snake. Four patients received antivenom. The regional venom response team offered management guidance and antivenom. One patient's hospitalization was protracted and worsened by respiratory failure and corneal dystrophies. All patients survived and were discharged.

Conclusions This series emphasizes the necessity of early and comprehensive management measures to reduce morbidity and mortality from snake envenomation, as well as the need for ongoing research and interventions to improve patient care in a variety of clinical settings.

Keywords Envenomation, antivenoms, snake venom, clinical care, snakebite management.

GESTIONAREA CLINICĂ A MUȘCĂTURILOR DE ȘARPE VENINOS: O SERIE DE CAZURI

Introducere În comunitățile rurale tropicale, mușcătura de șarpe veninos este una dintre principalele cauze ale morbidității și mortalității. Aceasta duce la șoc, hemoragii, necroză tisulară și edem. Diagnosticarea și identificarea speciilor de șerpi reprezintă o provocare, necesitând evaluări clinice amănunțite și teste de diagnostic la unitatea medicală primară. Astfel, această serie de cazuri analizează evoluția clinică și gestionarea cazurilor de mușcături de șarpe veninos în districtul Erode, India, o zonă cunoscută pentru șerpii de acest fel, precum Cobra indiană *(Naja naja)*, Vipera lui Russell *(Daboia russelii)* și Krait-ul comun *(Bungarus caeruleus)*.

Materiale și metode Această serie de cazuri rezumă experiența clinică a pacienților mușcați de un șarpe veninos, care au fost spitalizați la un Colegiu medical guvernamental și spital.

Rezultate Cinci pacienți au fost confirmați sau suspectați că au fost mușcați de un șarpe. Patru pacienți au primit ser antiviperin. Echipa regională specializată a oferit ghidaj pentru gestionarea cazurilor și administrarea de ser antiviperin. Spitalizarea unui pacient a fost prelungită din cauza insuficienței respiratorii și a distrofiilor corneene. Ca rezultat, toți pacienții au supraviețuit și au fost externați.

Concluzii Acest studiu subliniază necesitatea unor măsuri de gestionare precoce și completă pentru a reduce morbiditatea și mortalitatea cauzată de mușcăturile de șarpe veninos, precum și necesitatea unor cercetări și intervenții continue, pentru a îmbunătăți îngrijirea pacienților în diverse situații clinice.

Cuvinte cheie Mușcătura de șarpe, ser antiviperin, venin de șarpe, îngrijire clinică, gestionarea mușcăturii de șarpe.

ABBREVIATIONS:

ALKP – alkaline phosphatase;
ASV – anti-snake venom;
Bp – blood pressure;
CBC – complete blood count;
CRP – C-reactive protein;
CKMB – creatine kinase-myocardial band;
CK – creatine kinase;
HB – hemoglobin;
INR – international normalized ratio;
LDH – lactate dehydrogenase;
MCH – mean corpuscular hemoglobin;
MCHC – mean corpuscular hemoglobin concentration;
MCV – mean corpuscular volume;
PR – pulse rate;
PLT – platelet;
PT – prothrombin time;
RBC – red blood cell;
RBS – random blood sugar;
SGOT – serum glutamic-oxaloacetic transaminase;
SGPT – serum glutamic pyruvic transaminase;
SpO_2 – oxygen saturation;
WBC – white blood cell;
WBCT – whole blood clotting time;
WHO – World Health Organization.

INTRODUCTION

Snakebite is a major public health concern, especially in tropical and subtropical regions, with high morbidity and mortality rates. Every year, nearly 5 million snake bites occur worldwide, resulting in 20,000-25,000 mortalities (1). India, with its great biodiversity, has the highest incidence of snakebite-related mortalities, with estimates ranging from 35,000 to 50,000 each year (2). India's snake species include highly venomous snakes such as the spectacled cobra (*Naja naja*), Russell's viper (*Daboia russelii*), and the common krait (*Bungarus caeruleus*). These snakes are responsible for a considerable fraction of envenomations, which result in a variety of clinical symptoms such as neurotoxicity, hemotoxicity, and cytotoxicity (3,4). Snake venom is a complex combination of enzymes, proteins, and peptides that can induce local damage to tissues, coagulopathy, neurotoxicity, and renal failure (5). Snakebite envenomation must be managed effectively using a multidisciplinary strategy that involves immediate antivenom delivery, supportive care, and complications treatment. Antivenom therapy, produced from immunized animal plasma, is still the primary treatment option (6). The snake species responsible for the bite guides the choice of antivenom, necessitating accurate clinical examination and, in many cases, laboratory confirmation (7). Snakebites are common in Erode District, Tamil Nadu, with rural inhabitants frequently encountering venomous snakes. As per the international guidelines, the treatment of such snake envenomation is given in Appendix 2. The purpose of this case series is to describe and assess the clinical characteristics, diagnostic findings, treatment options, and outcomes of snakebite patients treated at Erode government medical college and hospital. By evaluating these cases, we seek to emphasize the difficulties in managing snake bites and make recommendations for improving patient treatment and outcomes in comparable settings.

CASE SERIES DESCRIPTION

Case 1: Suspected Krait Snake Bite

A 32-year-old female patient was admitted to the hospital with complaints of a snake bite over the right middle finger. The bitten snake was identified as krait. The patient was having complaints of severe pain, cellulitis, and swelling over the right hand around the fang marks. On examination, the patient was conscious, oriented, afebrile, and obeyed oral commands. Her vitals and laboratory parameters were found to be normal, as given in Ta-

ble 3. It was noted that Whole Blood Clotting Time (WBCT) was less than 20 mins and there was an absence of coagulopathy. Initially, the patient was administered Iv-line, Inj. Tetanus toxoid, Inj. Ceftriaxone 1 g for prevention and treatment of infection, and Inj. Ranitidine 50 mg as ulcer prophylaxis. T. paracetamol 500 mg and T. serratiopeptidase 10 mg were also administered for the management of pain and inflammation on the right hand. Anti-Snake Venom (ASV) was not administered to the patient. It was observed that cellulitis, edema, and severity of snake bite decreased by the next day. The patient was discharged on the 5th day of presentation. The clinical profiling, vitals, and laboratory parameters are given in Tables 1, 2, and 3 respectively.

Case 2: Probable Cobra Snake Bite

A 67-year-old male patient was admitted to the hospital with the reported history of a snake bite over the left foot dorsum. The patient was having complaints of giddiness, drooping of eyelids, and dyspnoea. The bitten snake identified as a cobra. The patient had a history of chronic alcohol use for the past 30 years. On general examination, he was drowsy and ptosis was present. In view of the impending respiratory failure, the patient was incubated with 8-mm-size Endotracheal Tube (ET. Tube), bilateral air entry was checked and was connected to mechanical ventilator. He was administered with 10 vials of ASV in 100 mL Normal saline over 1 hour. As there was no recurrence of ptosis, Inj. Adrenaline, Inj. Atropine 0.6 mg, and Inj. Neostigmine 0.4 mg were administered. During the laboratory investigation, Creatine Kinase (CK) and Lactate Dehydrogenase (LDH) values were elevated, and all other parameters are normal, as given in Table 3. The patient was further managed by the administration of Inj. Ranitidine 50 mg, Inj. Hydrocortisone 100 mg, Inj. Ondansetron 4 mg, and T. Chlorpheniramine 4 mg. Inj. Thiamine 100 mg was administered as the patient was diagnosed with alcohol dependence syndrome. Days later, the severity decreased, and the patient was discharged on the 6th day of admission. The clinical profiling, vitals, and laboratory parameters are given in Tables 1, 2, and 3 respectively.

Case 3: Unknown Snake Bite

A 16-year-old male patient was admitted to the hospital with the history of a snake bite and presented with complaints of pain and bleeding at the bite site, headache, and vomiting. The bitten snake was unknown. The pain radiates from the leg to the thigh. On local examination, diffuse pitting edema was present in the left leg from foot to thigh. Warmth, tenderness, and pulsation were present at the dorsum of the foot. The patient has no other comorbidities. On general examination, the patient obeys oral commands, and hydration was fair. On systemic examination, the patient was normal. During the laboratory investigation, it was found that the platelets were increased and Mean Corpuscular Volume (MCV) was decreased. The prothrombin time (PT) and International Normalized Ratio (INR) value were found to be slightly increased in the patient mentioned in Table 3. Immediately after admission, the patient was administered with injection ASV 8 vials in 1-pint normal saline over 1 hour along with Inj. cefotaxime 1 g, Inj. ondansetron 3 mg, Inj. Paracetamol 750 mg, and Inj. Ranitidine 50 mg. The child developed abdominal pain and wheezing while receiving antivenoms, and epinephrine was administered to treat an anaphylactic reaction. On the next day, Inj. Metronidazole 500 mg and T. Serratiopeptidase 10 mg were added for management of infection, inflammation, and pain. By the 7th day of admission, the symptoms decreased, and the patient was discharged by the next day. The clinical profiling, vitals, and laboratory parameters are given in Tables 1, 2, and 3 respectively.

Case 4: Respiratory Failure and Corneal Dystrophies

A 25-year-old male patient was presented to the emergency department with an alleged history of snake bite over the left foot 30 minutes prior to the presentation. The snake was unknown. He complained of giddiness and difficulty breathing and swallowing. On local examination, there was swelling and cellulitis over the left foot, along with a bite mark. On general examination, he was found to be drowsy, irritable, and disoriented, along with traumatic scarring of the cornea. Primarily, he was hypertensive, and a systemic examination was found to be unremarkable. In view of impending respiratory failure, the airways were secured by endotracheal intubation and mechanical ventilation. He was diagnosed to have local and neurotoxic signs of envenomation and was administered with 10 vials of injection ASV, followed by administration of injection atropine 0.6 mg, injection neostigmine 0.5 mg, and broad-spectrum antibiotics. T. paracetamol 500 mg and T. serratiopeptidase 10 mg were further administered for the management of pain and swelling. The patient condition gradually improved and was discharged on the 5th day of presentation. The clinical profiling, vitals, and laboratory parameters are given in Tables 1, 2, and 3 respectively.

Case 5: Snake Wrangler Case

A 55-year-old male patient was admitted to the hospital with complaints of a snake bite on the right leg. Local examination shows pain and swelling at the bite site in the middle of the right leg and cellulitis till the knee joint. Primarily the patient was hypertensive; otherwise, the systemic examinations were unremarkable. During the laboratory investigations, Mean Corpuscular Hemoglobin Concentration (MCHC) was found to be slightly elevated, as all the renal, liver, and clotting parameters are as per given in Table 3. Initially, the patient was administered with 8 vials of anti-snake venom, followed by administration of inj. ceftriaxone 1 g, inj. ranitidine 50 mg, T. paracetamol 500 mg, T. serratiopeptidase 10 mg, and T. chlorpheniramine 10 mg. Days after the patient was found to be normal and stable and was discharged on the 6th day of presentation. The clinical profiling, vitals, and laboratory parameters are given in Tables 1, 2, and 3 respectively.

Table 1. Clinical profiling of all the cases.

Case	Medical Condition	Symptoms	Comorbidities	Clinical Profile	Biochemical Profile	ASV	Clinical Outcome
1	Suspected krait bite	Severe pain, cellulitis, swelling Fang mark Edema	-	Female, 32 years old	Normal CBC, elevated CRP	-	Discharged on 5th day
2	Probable cobra bite	Fang mark Giddiness, drooping eyelids, dyspnoea	Alcoholic dependence syndrome	Male, 67 years old	Elevated WBC, normal electrolytes	Given	Discharged on 6th day
3	Unknown snake bite	Pain, bleeding, vomiting, headache	-	Male, 16 years old	Anaemia, normal electrolytes	Given	Discharged on 8th day
4	Unknown snake bite	Swelling, cellulitis, Respiratory failure, drowsy, irritable, disoriented, giddiness, dyspnoea, dysphagia corneal dystrophies	-	Male, 25 years old	Normal CBC, elevated CRP	Given	Discharged on 5th day
5	Unknown snake bite	Pain, swelling	-	Male, 55 years old	Normal CBC, elevated CRP	Given	Discharged on 6th day

Table 2. Vitals of cases.

Vitals	Case 1	Case 2	Case 3	Case 4	Case 5
Blood pressure (Bp) (mmHg)	130/90	130/90	109/68	150/97	140/90
Pulse Rate (PR) (bpm)	90	86	76	97	90
SpO2 (%)	97	97	100	99	98

Table 3. Laboratory investigations.

Parameters	Case 1	Case 2	Case 3	Case 4	Case 5
HB (g/dL)	12.6	14.8	13	16.2	14.1
RBC (10^{12}/L)	3.7	4.8	5.0	3.9	3.3
WBC (10^{9}/L)	7.5	6.9	10.6	6.21	6.4
PLT (10^{9}/L)	285	249	301*	265	249
MCHC (g/dL)	34	35.9	37.8*	33.4	37.4
MCH (pg)	28	27.5	29.4	26.1 -*	31.2
MCV (fL)	81	76.9 -*	77.8 -*	78.1 -*	83.4
RBS (mg/dL)	96	98	107	154*	NA
UREA (mg/dL)	18	20	15	26	30
CREATININE (mg/dL)	0.7	0.8	0.7	0.9	0.8
TOTAL PROTEIN (mg/dL)	7.5	7.6	7.5	7	7
ALBUMIN (g/dL)	3.8	3.6	4.3	3.7	4.3
TOTAL BILIRUBIN (mg/dL)	0.3	0.3	0.4	0.6	1.1
SGOT (IU/L)	29	46*	20	21	46*
SGPT (IU/L)	26	40	14	15	46
ALKP (IU/L)	78	174	223	112	63
CK (U/L)	NA	209**	NA	NA	NA
CKMB (U/L)	NA	96**	NA	NA	NA
LDH (U/L)	NA	440**	NA	NA	NA
Na +(mmol/L)	NA	NA	NA	142	NA
K +(mmol/L)	NA	NA	NA	3 -*	NA
PT (Seconds)	NA	10 -*	19.5**	14*	10.2 -*
INR (Seconds)	NA	0.71 -*	1.49**	1.03	0.73 -*
WBCT (Minutes)	<20 min	<20 min	<20 min	=20	<20 min

-*: slightly decreased; *: slightly elevated; **: highly elevated; **NA**: not assessed

MATERIALS AND METHODS

A case series study on snake bites was conducted at a tertiary care teaching hospital to examine the clinical course, management, and outcomes of snake envenomation. The study was conducted at the hospital's emergency department and intensive care unit over a one-year period, from June 2023 to June 2024. A thorough proposal for this study was presented to the institutional ethics committee of the government erode medical college and hospital, and approval was granted (IEC/2023/013). The study covered a total of five patients.

The management protocol followed was based on the standard guidelines recommended by World Health Organization (WHO). This study included patients of all ages and genders with a confirmed or highly suspected snake bite. Patients having a history of allergic reaction to antivenom and patients with insufficient medical records were excluded from this study (patients were excluded if their medical records were incomplete or lacked essential information such as diagnostic results, treatment history, or follow-up data). Data were obtained from medical records, which included demographic information, clinical presentation, treatment provided, laboratory findings, and clinical outcomes. The flow of case study was represented in figure 1.

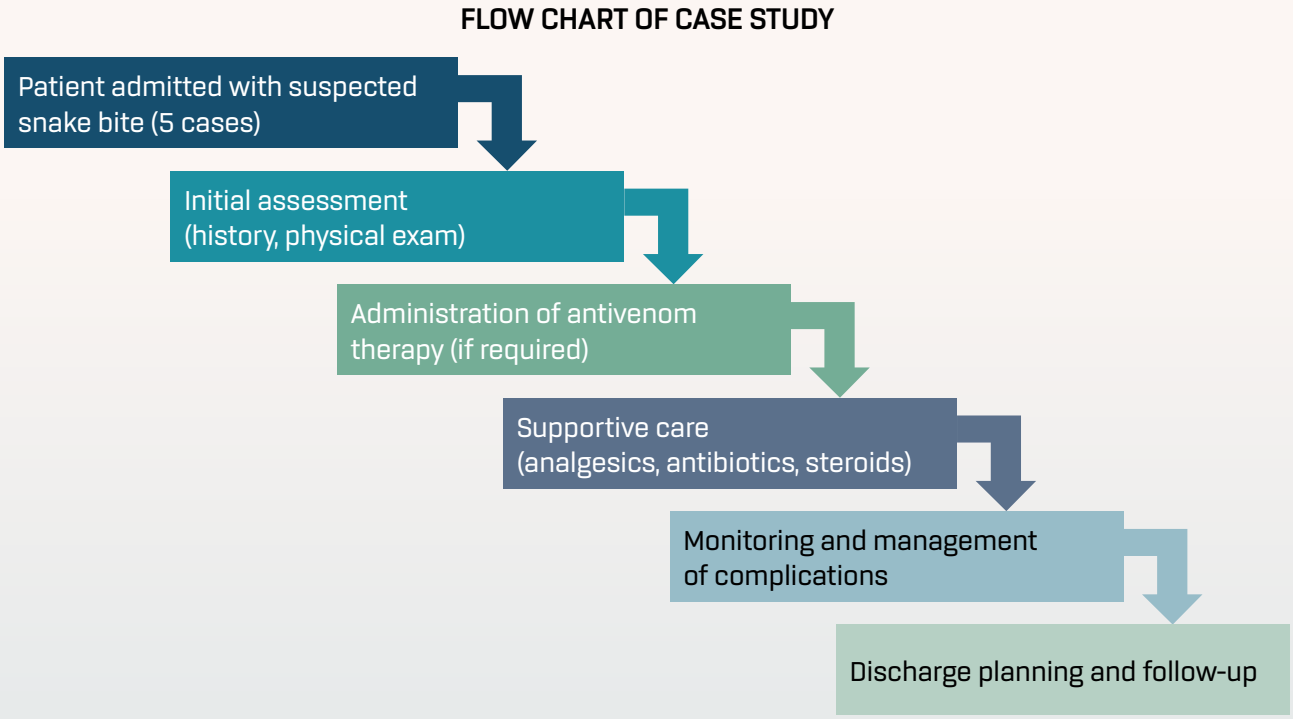

Figure 1. Chart of Case Series.

DISCUSSION

Snakebite remains a global health issue, with significant morbidity and mortality rates. Challenges in snake identification, particularly in rural settings, highlight the need for improved training and tools for accurate identification. First aid knowledge among the public is crucial for reducing complications. Most bites in this series affected the lower limbs, consistent with previous studies. The clinical signs and biochemical markers observed align with known effects of snake envenomation. The administration of antivenom, although associated with allergic reactions in some cases, remains the definitive treatment. Supportive care and patient-specific interventions are

essential for managing complications and comorbidities. The role of clinical care in optimizing treatment protocols and patient outcomes is significant. Snake envenomation remains a significant health problem globally, with substantial morbidity and mortality. The WHO estimates that over 5 million people are bitten by snakes each year, resulting in 20,000 to 25,000 mortalities, predominantly in rural and underserved populations (8). India, with its rich biodiversity, accounts for the highest number of snakebite-related mortalities globally, with estimates ranging between 35,000 and 50,000 deaths annually (9). This alarming statistic underscores the urgent need for effective management strategies and public health interventions to mitigate the impact of snakebites, particularly in rural and agricultural communities where the risk is highest (10).

The primary goal of snakebite management is to neutralize venom toxins and mitigate complications through the timely administration of antivenom. Polyvalent antivenoms, which target multiple venom components, are the standard treatment for snake envenomation in India (11). However, the use of antivenom is not without challenges, including the risk of hypersensitivity reactions and serum sickness. Despite these risks, antivenom remains the most effective treatment for snakebites, significantly reducing mortality and morbidity when administered promptly (12).

The clinical presentation of snake envenomation varies widely depending on the species involved, the amount of venom injected, and the site of the bite. Common symptoms include local pain and swelling, systemic manifestations such as nausea, vomiting, and neurological deficits, and laboratory abnormalities indicative of coagulopathy and organ dysfunction (13). Accurate identification of the offending snake species can be challenging, particularly in regions with high snake diversity and limited resources for species identification. This underscores the need for a high index of suspicion and a broad approach to management in areas where multiple venomous species are endemic (14).

CASE SERIES ANALYSIS

Case 1: Suspected Krait Snake Bite

In this case, the patient presented with localized symptoms of pain and swelling without systemic manifestations. The decision not to administer antivenom was based on the absence of systemic symptoms and normal biochemical parameters, including a whole blood clotting time of less than 20 minutes. The patient responded well to symptomatic treatment and antibiotics, highlighting the importance of clinical judgment in managing cases where the availability of antivenom is limited (15).

Case 2: Probable Cobra Snake Bite

This case involved a patient with significant systemic symptoms, including ptosis and respiratory difficulty, suggestive of neurotoxic envenomation likely from a cobra bite. The elevated levels of CK and LDH indicated muscle injury, which is consistent with cobra venom's known myotoxic effects. The administration of ten vials of antivenom resulted in a marked improvement in the patient's condition, emphasizing the critical role of antivenom in managing neurotoxic snakebites. The patient's mild residual ptosis at follow-up suggests partial recovery of neuromuscular function, which is a common outcome in neurotoxic envenomation (16).

Case 3: Unknown Snake Bite

In this case, the patient exhibited both localized and systemic symptoms, including bleeding and vomiting. The slightly prolonged PT and INR suggested a mild coagulopathy. The administration of eight vials of antivenom led to complete recovery, with no residual effects noted at one-year follow-up. This case underscores the importance of antivenom in managing both local and systemic effects of snake envenomation, even when the exact species is unknown (17).

Case 4: Respiratory Failure and Corneal Dystrophies

This patient presented with severe systemic symptoms, including respiratory failure and neurological deficits, indicative of a severe envenomation possibly from a cobra or krait. The development of corneal dystrophies as a complication is notable and highlights the need for comprehensive supportive care in managing the long-term sequelae of severe envenomation. The patient's prolonged hospital course and the need for respiratory support underscore the potential severity of neurotoxic snakebites and the critical role of antivenom in preventing fatal outcomes (18).

Case 5: Snake Wrangler Case

The patient in this case, a professional snake wrangler, experienced significant local reactions, including pain, swelling, and cellulitis, following a cobra bite. The timely application of a tourniquet and administration of antivenom and antibiotics resulted in a good outcome, with no residual effects at nine-month follow-up. This case highlights the importance of first aid measures and prompt medical intervention in reducing the severity of envenomation and preventing complications (19).

All the 5 cases were followed up and shown in appendix 1.

COMPARATIVE ANALYSIS

The outcomes observed in this case series are consistent with findings from previous studies conducted in India and other regions with high snakebite incidence. A study by S. Stephen et al. in Tamil Nadu reported a mortality rate of 2% among snakebite patients, with coagulopathy and renal failure being common complications (20). Another study by Halesha et al. in Karnataka found a 1.5% mortality rate, with neurotoxic symptoms and cellulitis frequently observed among snakebite victims (21). These findings shown in Table 4 underscore the variability in clinical outcomes and the critical role of timely and appropriate management in improving patient survival and recovery.

Table 4. Comparative Analysis with Previous Studies.

Study	Population	Common Snakes	Bites Analyzed	Antivenom Reaction Rate	Mortality Rate	Common Complications
Present Study	Erode District	Cobra, Krait, Russell's	5	20%	0%	Respiratory failure, cellulitis
S. Stephen et al. (2021)	Tamil Nadu	Cobra, Krait, Viper	100	15%	2%	Coagulopathy, renal failure
Halesha et al. (2013)	Karnataka	Cobra, Krait, Viper	75	10%	1.50%	Neurotoxic symptoms, cellulitis
Gupta et al. (2011)	Northern India	Cobra, Viper, Krait	50	12%	2.50%	Hemotoxic symptoms, infection

CONCLUSION

1. This case series highlights the diverse clinical presentations and outcomes associated with snake envenomation in Erode District, India.
2. The timely administration of antivenom, combined with supportive care and management of complications, is crucial in improving patient outcomes.
3. The variability in clinical manifestations and the challenges in species identification underscore the need for a multidisciplinary approach and ongoing research to optimize snakebite management protocols.

CONFLICT OF INTEREST The author does not declare any conflict of interest.

ETHICAL APPROVAL: A detailed proposal for this study was submitted to the institutional ethics committee of the government erode medical college and hospital, and approval was granted (IEC/2023/013).

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APPENDICES

Appendix 1. Follow-Up and Long-Term Outcomes.

Case No.	Follow-Up Duration	Residual Effects/Complications	Quality of Life Post-Discharge
1	6 months	None	Good
2	3 months	Mild ptosis	Fair
3	1 year	None	Excellent
4	6 months	Corneal dystrophies	Fair
5	9 months	None	Good

Appendix 2. Comparisons with International Guidelines.

Guideline	Recommendation	Present Study Findings
WHO Guidelines (2016)	Immediate antivenom administration	Administered within 2 hours of admission
Indian National Snakebite Protocol	Use of polyvalent antivenom	Polyvalent antivenom used in 4 cases except 1st case as there was no necessity to administer ASV.
UK Snakebite Management Protocol	Initial dose of 8-10 vials of antivenom	Doses of 8-10 vials used

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EXPERT OPINION – AVIS D'EXPERT

STRENGTHENING THE BIOLOGICAL WEAPONS CONVENTION IN SUPPORT OF GLOBAL PEACE AND SECURITY

Dr. Alex LAMPALZER

INTRODUCTION

On 26 March 2025, the Biological Weapons Convention (BWC) celebrated its fiftieth anniversary. Over the course of the last five decades, the BWC has established itself as one of the key pillars in multilateral disarmament. The BWC builds on the foundations of the 1925 Geneva Protocol, which prohibited only the use of biological and chemical weapons in warfare. The Convention goes beyond that by comprehensively banning an entire category of weapons of mass destruction. It effectively prohibits the development, production, stockpiling, acquisition, retention and use of biological weapons against humans, animals and plants.

Following its negotiation at the end of the 1960s and early 1970s in Geneva, Switzerland, the Convention was opened for signature on 10 April 1972 in London, Moscow and Washington D.C. It entered into force on 26 March 1975.

THE IMPLICATIONS OF ADVANCES IN SCIENCE AND TECHNOLOGY ON THE CONVENTION

As of 8 June 2025, 189 States have become party to the Convention. While its near universal adherence and the non-use of biological weapons by States must be considered great successes, constant vigilance is required to ensure that this established norm remains strong. Tremendous advances in the life sciences have brought many benefits to humankind, including the curing of diseases and the reduction of hunger and of poverty. At the same time and taking into consideration the dual use nature of life sciences and comparably easier access to relevant technology, equipment and materials nowadays, these scientific and technological breakthroughs have also lowered the threshold for the development of biological weapons. This is especially true for non-state actors. However, it should also be noted that the development of a sophisticated biological weapons programme still requires considerable expertise and major resources. Only international cooperation and multifaceted disarmament measures can ensure that advances are used peacefully and responsibly.

In an increasingly volatile international security landscape, where established disarmament norms face immense strain and potential risks continue to evolve, we must remain mindful that the threat of biological weapons has not been confined to history. The COVID-19 pandemic starkly demonstrated the devastating harm that the spread of infectious diseases can cause globally and the disruption that could be caused if biological agents were to be used deliberately as a weapon. This has only underscored the necessity of enhanced international efforts to further reinforce the Convention.

EFFORTS TO STRENGTHEN THE CONVENTION

In 2022, despite the challenging and increasingly volatile international security landscape, BWC States Parties were able to establish a new Working Group to 'identify, examine and develop specific and effective measures, including possible legally binding measures, and to make recommendations to strengthen and institutionalise the Convention in all its aspects'. The Working Group addresses various topics, including, *inter alia*, the issue of verification and compliance, as the Convention currently lacks a multilateral verification regime.

Intensive efforts to strengthen the BWC by creating a verification regime date back to the 1990s. Between 1992 and 1993, a group of experts assessed 21 potential verification measures from a scientific and technical point of view in four meetings (VEREX). The group concluded that some of these measures could contribute to strengthening the effectiveness as well as improving the implementation of the Convention. It was also stated that not a single measure, but a combination of them could contribute to improved verifiability. However, the subsequent negotiations on a legally binding Additional Protocol between 1995 and 2001 were ultimately unsuccessful and represented a major setback in the efforts to strengthen the Convention.

More than 30 years have passed since VEREX and enormous advances in the field of science and technology have enabled completely new verification methods, but at the same time also have presented some challenges. Various proposals are currently being discussed within the framework of the abovementioned Working Group. From today's perspective, the discussions on a potential verification regime for the BWC have made good progress. Although proposals differ between States Parties, there is a shared understanding that verification can strengthen the Convention. The discussions are currently still at an early stage and States Parties are exchanging national positions on the strategic goal and purpose of a verification regime for the BWC as well as its basic principles. The Working Group is requested to complete its work as soon as possible, preferably before the end of 2025.

ENHANCING NATIONAL IMPLEMENTATION OF THE CONVENTION

In the meantime, it remains vital to adopt and enforce comprehensive biosafety and biosecurity measures at the national level. In early 2025, the Republic of Moldova, which acceded to the BWC on 28 January 2005, designated the National Agency for Public Health as the country's BWC National Contact Point (NCP). The NCP is responsible for coordinating respective efforts at the national level. In this regard, close collaboration between a range of stakeholders, including the scientific and technical community, policy makers and civil society is crucial.

The Republic of Moldova regularly participates in BWC meetings in Geneva and has also taken up active roles and functions during previous Review Conferences. Of note, at the Ninth BWC Review Conference in 2022 Ambassador Tatiana Molcean chaired the Committee of the Whole. Likewise, at the Eighth BWC Review Conference in 2016, Ambassador Tudor Ulianovschi chaired the Credentials Committee.

The Republic of Moldova also frequently submits the annual Confidence-Building Measures (CBMs) reports. Since its accession in 2005, Moldova has submitted 14 national reports that inform about relevant national bio-capacities

and activities. The country thus contributes to the overarching aim of CBMs in the framework of the BWC, namely to "prevent or reduce the occurrence of ambiguities, doubts and suspicions, and in order to improve international co-operation in the field of peaceful bacteriological (biological) activities".

CONCLUSION

The Biological Weapons Convention entered into force five decades ago in 1975. Back then, it was not possible to foresee whether the BWC would be able to meet the expectations placed on it. Although States Parties have been aware of the obvious weaknesses of the Convention – the lack of an international verification regime and an independent international organisation to facilitate the BWC's implementation – the Convention must nevertheless be considered as a success story. No State today publicly admits to possessing biological weapons nor are they an integral part in national military doctrines. Biological weapons have become 'outlawed weapons' and 189 states have joined the Convention. None of this could be expected or judged as a "given" in 1975.

It is hoped that the efforts in the framework of the Working Group will succeed and lead to a strengthened Convention. A Convention, that is fit for purpose and can continue to serve in the future as a strong norm and bulwark against weaponizing biology and making them unthinkable.

REQUIREMENTS FOR AUTHORS

Rules of drafting

The manuscript (written in English and French) should be in accordance with the guidelines published in: *Uniform Requirements for Manuscripts Submitted to Biomedical Journal (1994) Lancet 1996, 348, V2; 1-4* (www.icmje.org). The manuscripts should be written in font Cambria, size 11 points, spaced at 1.0, fully justified alignment, fields 2 cm on all sides. All pages must be numbered consecutively (in the right bottom corner) and continuously. Abbreviations should be explained at first occurrence in the text and should not be excessively used. The manuscripts must not exceed the number of words (without the title, affiliation, abstract and references): review articles – 4,500 words; research articles – 3,000 words; expert opinions – 2,500 words; case presentation – 1,700 words; experimental and clinical notes – 1,300 words; book reviews and presentations – 2,000 words; teaching articles – 4,000 words. The volume of tables and figures should not exceed 1/3 from the volume of the manuscript. The journal reserves the right to make any other formatting changes. Rejected manuscripts are not returned.

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The title should be as short as possible (maximum – 120 signs with spaces), relevant for the manuscript content. The names of the authors should be written in full: name, surname (*e.g.:* Jon JONES). Affiliation should include: Department/Unit/Chair, University/Hospital, City, Country of each author. Beneath the affiliation, the author`s details and contact information – e-mail address (*e.g.:* corresponding author: Jon Jones, e-mail: jon.jones@gmail.com).

The structure of the manuscript

The manuscript should comprise the following sub- headings (capitalized):

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- **MATERIAL AND METHODS**
- **RESULTS**
- **DISCUSSIONS**
- **CONCLUSIONS**
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- **ACKNOWLEDGEMENT** (optional)
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The **summary** should contain 1,600 signs with spaces:

- **Introduction**
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The summary should not include tables, charts, and bibliographic notes; information not included in the article.

Figures. The text included in figures should be written in font Cambria, 10 point. Each figure should be accompanied by a heading and legend. They should be numbered with Arabic numerals and placed in parentheses (*e.g.:* fig. 1). Both the title (*e.g.* Figure 1) and legend are centred, below the figure.

Tables. The text included in tables should be written in font Cambria, 10 point. Each table should be accompanied by a heading. Tables should be inserted into the text and adjusted to the width of the page. The tables are numbered in Arabic numerals and mentioned in body text in parentheses (*e.g.* tab. 1). The title of the table is centred on the top of the table (*e.g.* Table 1).

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Pregătirea manuscrisului (elaborat în limbile engleză și franceză) va fi în conformitate cu instrucțiunile publicate în: *Uniform Requirements for Manuscripts Submitted to Biomedical Journals (1994) Lancet 1996, 348, V2; 1-4* (www.icmje.org). Manuscrisele trebuie să fie cu font Cambria, dimensiune 11 puncte, spațiat la interval 1,0, aliniere justificată, câmpurile 2 cm pe toate laturile. Toate paginile trebuie să fie numerotate consecutiv (în colțul de jos, în partea dreaptă) și să includă numerotarea continuă a paginilor. Abrevierile trebuie să fie explicate la prima apariție în text și nu trebuie utilizate excesiv. Manuscrisele nu trebuie să depășească (fără a număra titlul, afilierea, rezumatul și referințele): pentru articole de sinteză/referate – 4500 de cuvinte; pentru articole de cercetare – 3000 de cuvinte; pentru opinii ale experților – 2500 de cuvinte; prezentare de caz și imagini din practica clinică/laborator – 1700 de cuvinte; note experimentale și clinice – 1300 de cuvinte; recenzii și prezentări de carte – 2000 de cuvinte; articole didactice – 4000 de cuvinte. Volumul tabelelor și figurilor nu trebuie să depășească 1/3 din volumul manuscrisului. Revista își rezervă dreptul de a face orice alte modificări de formatare. Manuscrisele respinse nu sunt returnate.

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Titlul ar trebui să fie cât mai scurt posibil (maximum – 120 de semne cu spații), elocvent pentru conținutul manuscrisului. Numele autorilor vor fi scrise deplin: prenume, nume de familie (*ex:* Ion RUSU). Afilierea va include: Secția/Departamentul/Catedra, Universitatea/Spitalul, Orașul, Țara pentru fiecare autor. Se vor menționa obligatoriu, mai jos, datele autorului corespondent și informațiile de contact – adresa de e-mail (*ex:* autor corespondent: Ion Rusu, e-mail: ion.rusu@gmail.com).

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Manuscrisul va cuprinde următoarele subtitluri (scrise cu majuscule):

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Figuri. Textul inclus în figuri trebuie să fie scris cu font Cambria, dimensiune 10 puncte. Fiecare figură trebuie să fie însoțită de titlu și legendă. Ele vor fi numerotate cu cifre arabe și vor fi menționate în text în paranteze (*ex:* fig. 1). Titlul (*ex:* Figura 1) și legenda figurii trebuie să fie scrisă centrat, sub figură.

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Tous les manuscrits à publier doivent être accompagnés par deux résumés: dans la langue originale et en anglais.

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Le titre doit être le plus court que possible (maximum – 120 signes avec espaces), éloquent pour le contenu du manuscrit. Les noms des auteurs seront écrits complets: prénom, nom (*ex:* Albert LEBRUN). Quant à l'affiliation, on devra indiquer: Section/Département/Chaire, Université/Hôpital, Ville, Pays – pour chaque auteur. Les données de l'auteur correspondant et les coordonnées – adresse e-mail (*ex:* auteur correspondant: Albert Lebrun, e-mail: albert.lebrun@gmail.com) seront obligatoires ci-dessous.

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Le manuscrit comprendra les sous-titres suivants (avec lettres majuscules):

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- **METHODES**
- **RESULTATS**
- **DISCUSSIONS**
- **CONCLUSIONS**
- **CONFLIT D'INTERETS**
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Le **résumé** contiendra 1600 signes avec espaces:

- **Introduction**
- **Méthodes**
- **Résultats**
- **Conclusions**
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Le résumé ne comprendra pas des tableaux, graphiques et des notes bibliographiques; des informations non présentées dans l'étude.

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The *One Health* concept

Globally, the One Health concept is a worldwide strategy to expand interdisciplinary collaborations and communications in all aspects related to the health care of humans, domestic animals or wildlife, which can no longer be approached separately, but only jointly.

One Health addresses not only human and animal disease concerns, but also issues related to lifestyle, diet, exercise, the impact of different types of human-animal relationships, and environmental exposures that can affect both populations. In order to achieve the expected effects, it is also necessary to educate the population to make them aware of the risk factors and benefits of prevention, as well as communication and understanding between patients and healthcare providers.

HUMAN HEALTH

The WHO defined health in 1946 as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity", with the later addition of "the capacity to lead a socially and economically productive life".

ANIMAL HEALTH

The OIE defines animal welfare in 2008: an animal is in good condition if it is healthy, enjoys comfort, is well fed, is safe, is able to display its innate (natural) behavior and does not suffer from unpleasant conditions such as pain, fear and stress.

PLANT AND ENVIROMENTAL HEALTH

Environmental health refers to those aspects of human health that include the quality of life determined by physical, biological, socio-economic and psycho-social factors in the environment. The interrelationships of people with the environment concern medicine, when an ecological system is in a state of equilibrium, the health of the population prevails.


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