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Characteristics of salmonellosis pathogens circulating in Primorsky Krai before and during the COVID-19 pandemic

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Abstract

Introduction. To date, among intestinal infections, salmonellosis is a pressing health problem worldwide, including in the Russian Federation, causing acute infectious outbreaks of disease.

Objective of the study: to assess the impact of the COVID-19 pandemic on the epidemiological patterns and molecular biological characteristics of salmonella infection in Primorsky Krai for 2019–2023.

Materials and methods. A retrospective epidemiological analysis of salmonellosis incidence during the COVID-19 pandemic in the population of Primorsky Krai was conducted. Plasmid characteristics of non-typhoidal *Salmonella* strains and their serotype were established using alkaline lysis and serological typing methods.

Results. During the COVID-19 pandemic, both in the Russian Federation and in Primorsky Krai, the registration of salmonellosis was significantly lower than in the pre-pandemic period, and the seasonality of salmonellosis shifted to the autumn months. An inverse relationship of medium strength was revealed between the monthly incidence of salmonellosis and COVID-19. No significant changes in the plasmid spectrum and in the proportion of registration by serogroups and serotypes of *Salmonella* were observed. It was shown that salmonellosis infection in Primorsky Krai is mainly caused by *S. enteritidis* strains with a plasmid characteristic of 38 MDa, 38:1.4 MDa, 38:2.3 MDa, 38:4.4 MDa, rare variants of plasmid types were also detected, the influence of the COVID-19 pandemic on the emergence of new plasmid types has not been established.

Conclusion. The presented results of the study on the molecular biological characteristics of *Salmonella* circulating in Primorsky Krai during the COVID-19 pandemic will open up prospects for understanding the ecological and epidemiological patterns of the development of the epidemic process of salmonella infection.

Keywords: salmonellosis, *Salmonella*, serogroup, serotype, plasmid type, COVID-19 pandemic, SARS-CoV-2 virus

Ethical approval. The study was conducted with the informed consent of patients. The research protocol was approved by the Ethics Committee of the Somov Research Institute of Epidemiology and Microbiology of Rospotrebnadzor (protocol No. 3 February 03.2022).

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Характеристика возбудителей сальмонеллёзов, циркулирующих в Приморском крае до и во время пандемии COVID-19

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Аннотация

Введение. Сальмонеллёзы, для которых характерны острые вспышки заболеваемости, являются актуальной проблемой для здравоохранения.

Цель исследования: оценить влияние пандемии COVID-19 на эпидемиологические закономерности и молекулярно-биологические характеристики сальмонеллёзных инфекций в Приморском крае за 2019–2023 гг.

Материалы и методы. Проведён ретроспективный эпидемиологический анализ заболеваемости населения Приморского края сальмонеллёзами в период пандемии COVID-19. Методами щелочного лизиса и серологического типирования установлены плазмидная характеристика штаммов нетифоидных *Salmonella* и их серотип.

Результаты. Во время пандемии COVID-19 как в России, так и в Приморском крае регистрация сальмонеллёзов была значительно ниже, чем в допандемический период, а сезонность сальмонеллёзов сдвинулась на осенние месяцы. Выявлена обратная связь средней силы между данными помесечной заболеваемости сальмонеллёзами и COVID-19. Особых изменений в плазмидном спектре и в доле регистрации по серогруппам и серотипам *Salmonella* не наблюдалось. Показано, что сальмонеллёзные инфекции в Приморском крае в основном вызваны штаммами *S. enteritidis* с плазмидной характеристикой 38 МДа, 38:1,4 МДа, 38:2,3 МДа, 38:4,4 МДа, выявлялись также редкие варианты плазмидных типов. Влияние пандемии COVID-19 на появление новых плазмидных типов не установлено.

Заключение. Представленные результаты исследования об эпидемиологической и молекулярно-биологической характеристике *Salmonella*, циркулирующей в Приморском крае в период пандемии COVID-19, открывают перспективы для понимания эколого-эпидемиологических закономерностей развития эпидемического процесса сальмонеллёзов.

Ключевые слова: сальмонеллёз, *Salmonella*, серогруппа, серотип, плазмидный тип, пандемия COVID-19, вирус SARS-CoV-2

Этическое утверждение. Исследование проводилось при добровольном информированном согласии пациентов. Протокол исследования одобрен Этическим комитетом НИИЭМ им. Г.П. Сомова (протокол № 3 от 03.02.2022).

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Introduction

Salmonellosis are caused by various serotypes of bacteria of the genus *Salmonella*, are classified as poly-etiological infectious diseases in humans and animals, and pose a significant public health problem worldwide, contributing to an increased economic burden. Depending on the health status of the host organism and the serotype of *Salmonella*, as well as the bacteria's resistance to antimicrobial agents, 11–20 million cases of salmonellosis are registered worldwide annually, resulting in up to 161,000 deaths [1].

Nowadays, salmonellosis is one of the most common bacterial intestinal infections, with a trend towards increasing outbreaks of the disease. According to official statistics, in recent years, the average incidence rate in Russia was 13.61 per 100,000 population in 2021¹, 17.1 in 2022, and 21.45 in 2023, with the rate in certain territorial districts exceeding the national average.

In the Primorsky Krai over the past decade, against the background of significant changes in the etiological structure of intestinal infections towards an increase in the share of rotavirus and norovirus infections and a decrease in the proportion of diseases such as viral hepatitis A and E and shigellosis, the percentage of salmonellosis has practically not changed and fluctuates within 10% [2].

In 2020, an emergency situation arose due to the development of the COVID-19 pandemic caused by the SARS-CoV-2 virus, which significantly affected the incidence of other infectious diseases with various transmission mechanisms [3–9]. The literature mainly presents studies showing the impact of COVID-19 on acute respi-

ratory viral infections. Only a few publications address the impact of the COVID-19 pandemic on the epidemiological patterns and microbiological characteristics of infections related to the intestinal group [4], while there is virtually no data on its influence on the epidemiological patterns of salmonellosis development in Russia.

The aim of the study is to assess the impact of the COVID-19 pandemic on the epidemiological patterns and molecular-biological characteristics of non-typhoidal salmonellosis in the Primorsky Krai from 2019 to 2023.

Materials and methods

A retrospective epidemiological analysis of the incidence of salmonellosis and COVID-19 among the population of Primorsky Krai was conducted based on data from the federal state statistical observation for Primorsky Krai — "Information on Infectious and Parasitic Diseases" (Form No. 2) for the years 2009–2023.

The spectrum of plasmid types in salmonella strains was determined by the alkaline lysis method [10]. Known plasmid types RP4 (38 MDa), pBR322 (2.9 MDa), pVM82 (82 MDa) were used as molecular weight standards.

When performing the serological typing method, diagnostic salmonellosis adsorbed dry sera for agglutination reaction (Petsal) were used in accordance with the Kaufmann–White antigenic scheme [11].

Statistical data processing was carried out using the Microsoft Excel 2010 and Statistica v. 10 programs. The critical significance level p for testing statistical hypotheses was set at 0.05.

Results

The period from 2009 to 2012 in the Primorsky Krai was characterized by an increase in the incidence

¹ On the state of sanitary and epidemiological welfare of the population in the Russian Federation in 2023: State Report. Moscow; 2024. 368 p.

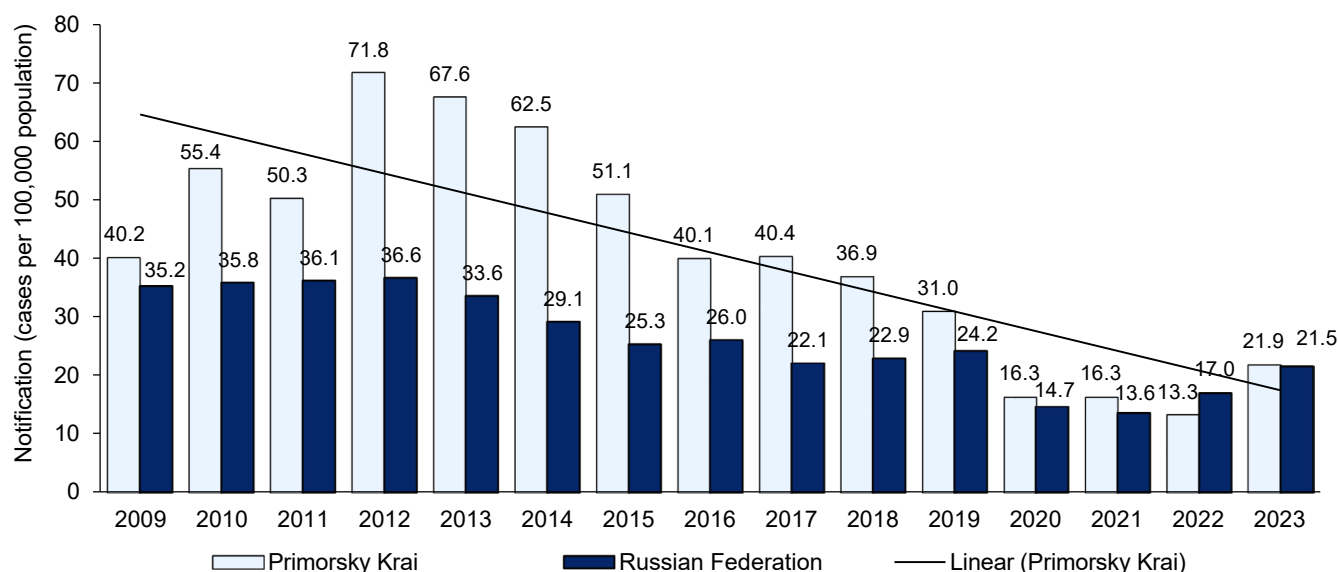


Fig. 1. The dynamics of salmonellosis incidence in Primorsky Krai and the Russian Federation in 2009–2023.

of salmonellosis, with a peak registered in 2012 at 71.8 per 100,000 population. In the following years, a trend towards a decrease in morbidity was observed, and by 2022, its level had dropped to 13.3 per 100,000 population (the growth rate was -4.2), whereas in Russia, the incidence of salmonellosis was more stable (the growth rate was -3.4). At the same time, the incidence rates in Primorsky Krai exceeded the national data from 2009 to 2019, and starting from 2020, they almost leveled off (**Fig. 1**). In 2023, an increase in morbidity was observed both in Primorsky Krai and in Russia as a whole (up to 21.6 per 100,000 population).

Before and during the COVID-19 pandemic, the lowest incidence of salmonellosis infections in the Primorsky Krai region was recorded in the municipal dis-

tricts of Terneisky, Kavalerovsky, Lazovsky, Olginsky, Partizansky, and the city of Fokino (**Fig. 2**). It should be noted that during the peak of the pandemic, *S. enterica* strains were not isolated in these areas.

A high level of salmonellosis, both before and during the COVID-19 pandemic, was recorded in the cities of Vladivostok, Ussuriysk, Spassk-Dalny, and in the Khorolsky and Khasansky districts. The period of maximum disease incidence occurred in 2019, and in 2023, a gradual recovery to the usual level was recorded.

In the monthly dynamics (**Fig. 3**), the incidence of salmonellosis before and during the COVID-19 pandemic from 2018 to 2019 was predominantly recorded in the summer-autumn period (June–October). At the

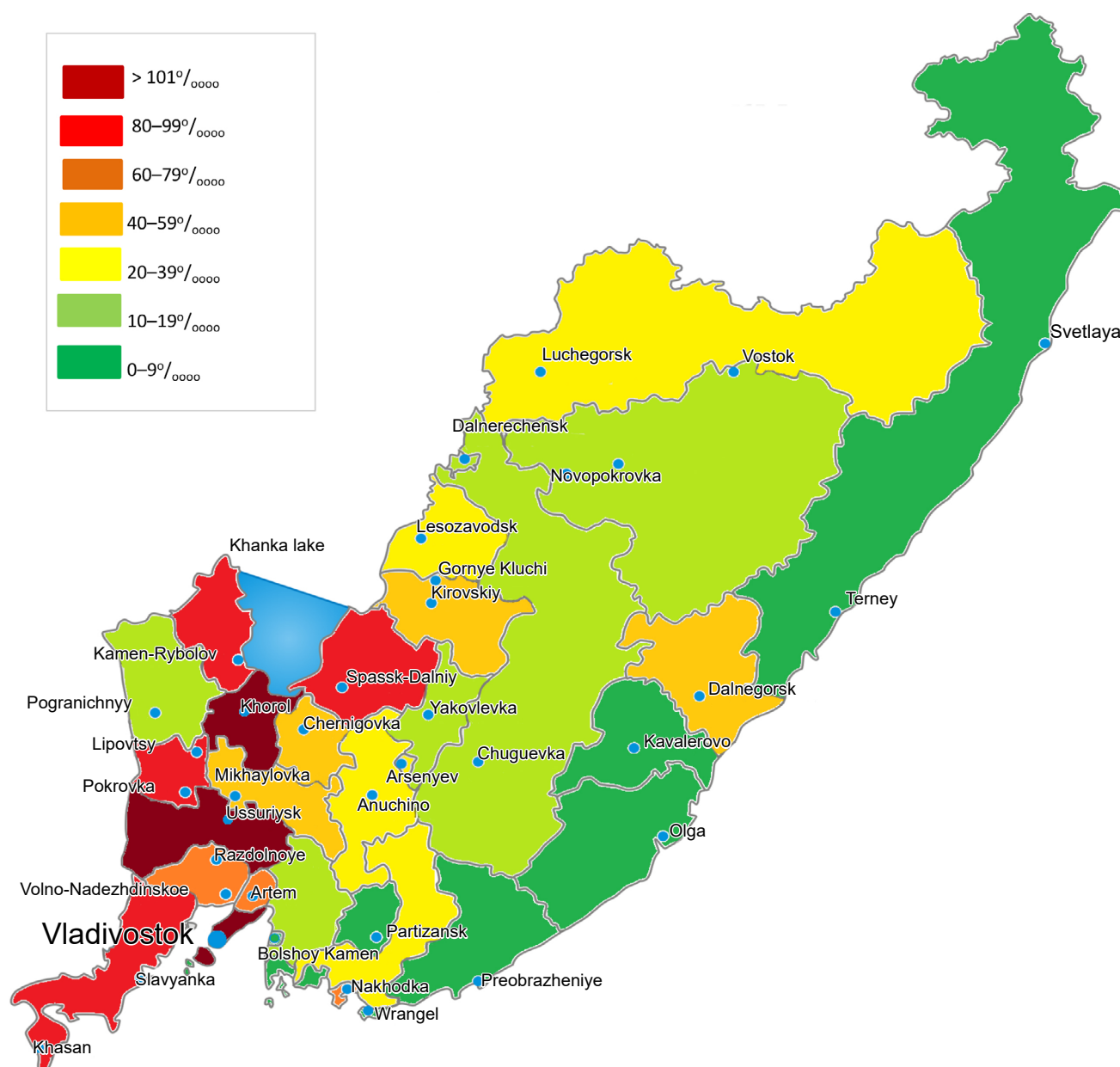


Fig. 2. Incidence of salmonellosis in the administrative territories of Primorsky Krai in 2019–2023 (per 100,000 population).

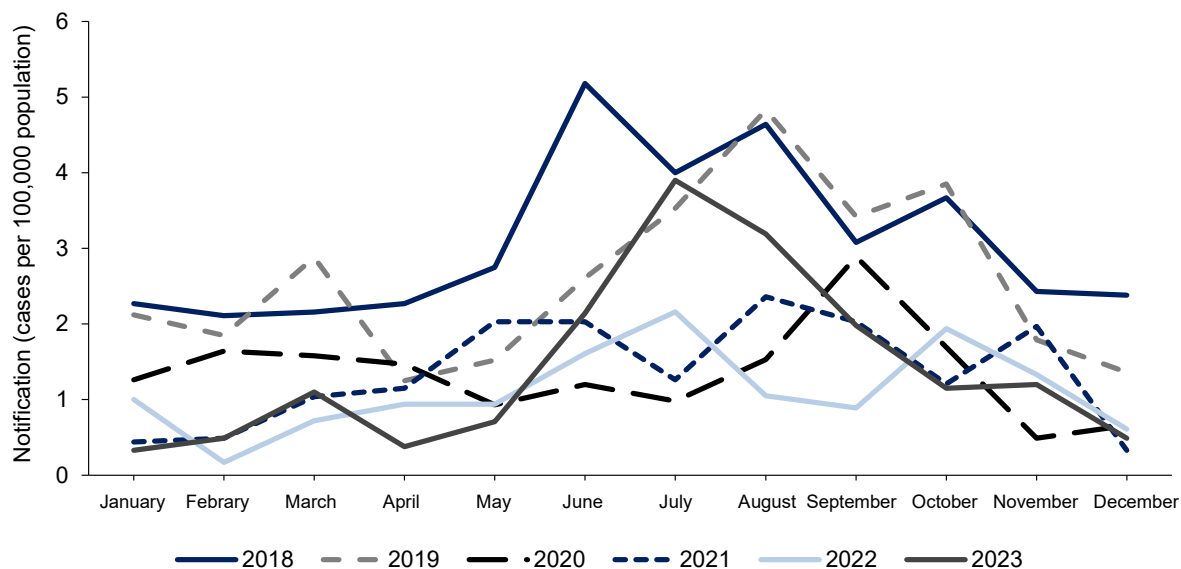


Fig. 3. Monthly dynamics of salmonellosis incidence in Primorsky Krai from 2018 to 2023.

height of the COVID-19 pandemic, starting in 2020, the seasonality shifted to the autumn months (September–October). In 2021, the highest peaks of salmonellosis incidence occurred in May and June, August and September, as well as November. In 2023, the incidence of salmonellosis in the Primorsky Krai region began to recover, and its seasonality was observed in the summer-autumn period (June–October). Similar results are reported by other authors as well [4].

Interesting data were obtained from the joint analysis of monthly COVID-19 morbidity in the same years. Thus, in the dynamics of COVID-19 and salmonellosis incidence for the years 2021–2022 (Fig. 4), four periods can be identified in the change of incidence levels. From January to October 2021, there was a decline in COVID-19 cases, while the incidence of salmonellosis increased. From November 2021 to March 2022, the incidence of COVID-19 increased, while the incidence of salmonellosis decreased from December 2021 to February 2022. From March to July 2022, there was a significant increase in the incidence of salmonellosis. From August to September 2022, there was an increase in COVID-19 cases alongside a decrease in reported salmonellosis cases. Correlation analysis of the presented data using Spearman's method revealed

a moderate inverse relationship between the monthly incidence data for both infections ($r = 0.5$; $p < 0.05$).

It has been established that in the Primorsky Krai, as well as in most regions of the Russian Federation and worldwide, *Salmonella* of serogroup D with the dominant *S. enteritidis* serotype holds the leading position, followed by serogroups C and B with insignificant share values (serogroup B — $9.1 \pm 1.3\%$; serogroup C — $9.7 \pm 1.3\%$). The last place is occupied by serogroup E, which was not registered in 2022. It should be noted that the lowest incidence of disease caused by other serogroups of *S. enterica* was recorded in 2022 (Fig. 5).

Nowadays, the main serotypes identified in salmonellosis are *S. enteritidis*, *S. typhimurium* and *S. infantis*. Since 1995 and up to the present, despite the diversity of plasmid types in the leading serotype *S. enteritidis*, the three main plasmid types — 38, 38:1.4, and 38:4.4 MDa—continue to hold prevalent significance (Table). Other, less frequently isolated plasmid types (38:2.3, 38:2.3:1.4, 38:2.6:1.4, 38:2.6:14, 38:3.0:1.4, 38:30, 38:30:1.4, 38:30:2.3 MDa — epidemic pool) have also retained their significance in shaping the epidemic situation. The results of the study showed that the number of salmonellosis cases caused by *S. enteritidis* with

Dynamics of the number of plasmid types of *S. enteritidis* isolated in the Primorsky Krai from 2009 to 2023

Plasmid types (MDa)	Year															Total strains	Isolate source
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023		
38	220	128	110	397	313	234	211	140	93	76	96	41	31	37	26	2153	v, fp, env.
38:1.4	297	323	299	343	538	349	309	154	186	138	66	17	17	12	17	3065	v, fp, env.
38:2.3	7	5	9	12	8	2	5	7	13	10	11	9	3	2	–	103	v, fp, env.
38:4.4	82	368	267	179	111	132	107	137	119	82	50	13	24	1	8	1760	v, fp

Note. v — patients; fp — food products; env. — environment.

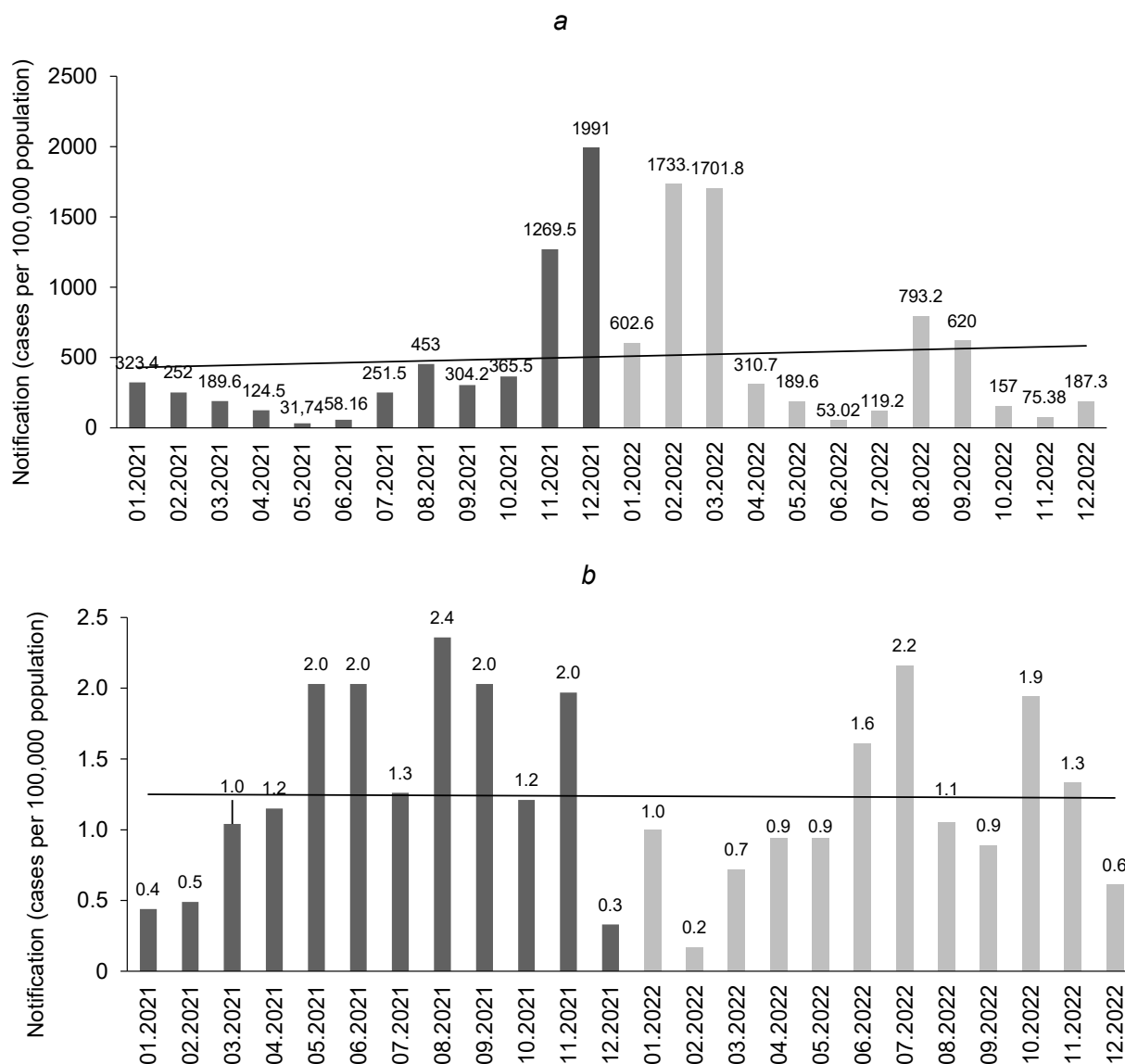


Fig. 4. Comparative analysis of the monthly dynamics of COVID-19 (a) and salmonellosis (b) incidence from 2021 to 2022.

plasmid types 38, 38:1.4, 38:2.3, and 38:4.4 MDa gradually decreased until 2019, and since the beginning of the COVID-19 pandemic, it has been reduced by half (Table 1).

It is important to note that both before and during the COVID-19 pandemic, rare plasmid type variants of the *S. enteritidis* serovar were identified: 38:26:2.6, 3.2:2.0, 38:3.8:3.0, 5.6:3.8:3.2:2.0, 38:4.4:3.2 50:38:20, 38:5.0:3.8:3.0, and 50:8.0:4.0:3.5:1.4 MDa. The impact of the epidemiological situation during the COVID-19 pandemic on the emergence of new plasmid types has not been established by us.

The second most significant serotype in the etiology of salmonellosis in the Primorsky Krai is *S. typhimurium*. From 2019 to 2023, more than 90 strains of *S. typhimurium* isolated from various sources were studied. All infections were of a foodborne nature, and no hospital strains were isolated. The most frequent-

ly registered strains were those with a single plasmid type — 60 MDa (14.3%), followed by the plasmid type 4.0:3.2 MDa (13.2%), which first appeared in 2015 (isolated from a patient in the city of Ussuriysk).

In the *S. infantis* serotype circulating in the Primorsky Krai region, the 100 MDa plasmid type predominated (72%), isolated from food products. Strains with other plasmid types were rarely isolated.

Discussion

Intestinal infections are a pressing issue worldwide due to the extremely widespread nature of this pathology, high morbidity rates, and, consequently, significant economic damage [12].

Salmonella infections and COVID-19 have different modes of transmission, but in some cases, they exhibit comparable symptoms [13, 14]. Moreover, the immunological response triggered by the SARS-CoV-2

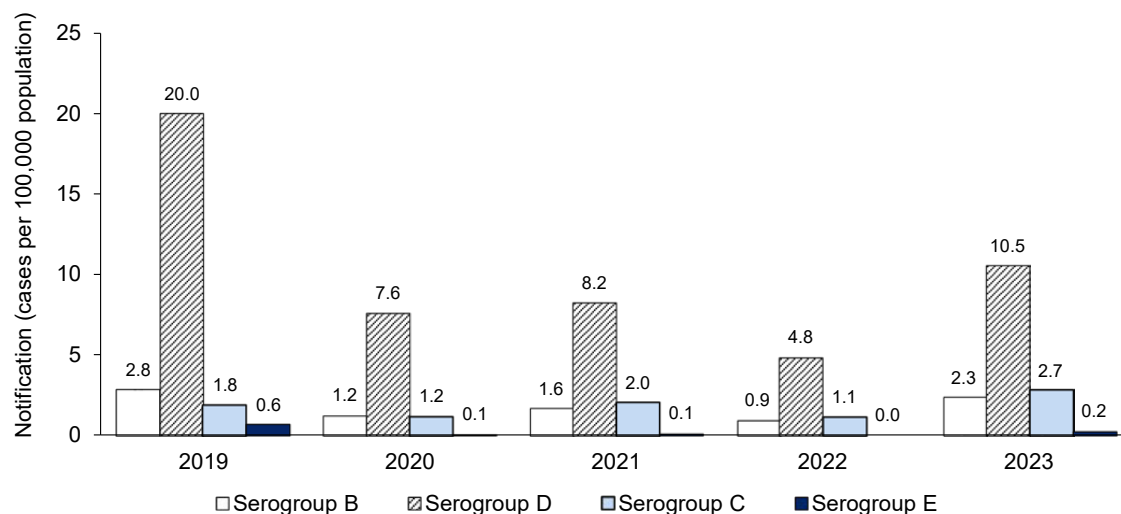


Fig. 5. Dynamics of the incidence of the population with individual serogroups of *Salmonella enterica* in Primorsky Krai from 2019 to 2023.

virus can influence the severity of bacterial infections, including salmonellosis [15]. It was later established that these factors have serious implications related to the onset and treatment of salmonellosis [16–19]. Cases of co-infection with *Salmonella* and COVID-19 have been reported in 9 studies worldwide [20], some of which were found in patients from Pakistan [21], Turkey [22] and Japan [23]. Patients with coinfection face more severe consequences and increase the complexity of therapeutic decisions necessary to address this issue.

In 2020, the development of the COVID-19 pandemic worldwide significantly affected the incidence rates of other infections with different transmission mechanisms. Thus, when comparing with the average annual indicator from 2016 to 2023, the incidence of infections with an aerosol transmission mechanism from 2020 to 2023 in Primorsky Krai was higher than the long-term average, while the incidence of intestinal infections was significantly lower. The lowest rates were recorded in 2020–2021, however, in the following years, there is a trend towards an increase.

The incidence rates of vector-borne infections for 2020–2023 were also significantly lower than the multi-year average. Similar data were obtained for the incidence of infections transmitted due to person-to-person contact.

It has been established that in all groups, except for air-borne infections, the incidence during the COVID-19 pandemic years, compared to the average indicators of previous years, has significantly decreased.

Salmonellosis in the Primorsky Krai continue to play an important role in shaping infectious morbidity, as evidenced by the increase in outbreaks and the exceedance of the average morbidity rate compared to Russia as a whole. It should be noted that during the peak of the COVID-19 pandemic, there was a decrease

in the growth of salmonellosis cases. The lowest incidence was registered in the Terneysky, Kavalerovsky, Lazovsky, Olginsky, Partizansky districts and Fokino, however, in the cities of Vladivostok, Ussuriysk, Spassk-Dalny, Khorolsky, and Khasansky districts, a high level of salmonellosis was noted. During the pandemic, a divergent trend was observed in the monthly dynamics of COVID-19 and salmonellosis incidence compared to the pre-pandemic period. The decrease in the registration of salmonellosis cases may be related to the isolation of the population during the pandemic, the transition to remote work formats, the quarantine of multidisciplinary medical organizations due to the detection of coronavirus infection cases, and the re-profiling of clinical hospitals for the diagnosis and specialized treatment of patients with confirmed diagnoses. Nevertheless, the influence of the biogeocenosis on the self-regulation of various microorganisms as a result of integrative-competitive relationships between them, which is reflected in the changing trends in the dynamics of morbidity from specific infections and the structure of infectious pathology, cannot be excluded in the formation of the existing epidemiological situation [24, 25].

Despite the diversity of plasmid types in the leading serotype *S. enteritidis*, three main plasmid types — 38, 38:1.4, and 38:4.4 MDa — play a dominant role in the development of salmonellosis, as confirmed by the research results. It has been established that salmonellosis infections in the Primorsky Krai, both in the pre-pandemic period and at the height of the COVID-19 pandemic, were mainly caused by *S. enteritidis* strains with plasmid characteristics of 38, 38:1.4, 38:2.3, and 38:4.4 MDa. Much like in the pre-pandemic period, rare variants of plasmid types were also identified. The impact of the epidemic situation during the COVID-19 pandemic on the emergence of new plasmid types has not been established.

Conclusion

The obtained data on the epidemiological and molecular-biological characteristics of the pathogens of salmonellosis circulating in the Primorsky Krai during the pre-pandemic period and at the height of the COVID-19 pandemic open up prospects for uncovering the ecological and epidemiological patterns of the epidemic process, which will allow for making informed managerial decisions for implementing control over salmonellosis infection.

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