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Epidemiology Survey of Measles in Kazakhstan

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Abstract

BACKGROUND: Measles (rubella) is a highly contagious disease that is caused by a virus in the Paramyxoviridae family. The measles virus is directly responsible for more than 100,000 deaths each year. Epidemiological studies have linked measles to increased morbidity and mortality many years after infection, but the reasons underlying this phenomenon are poorly understood. The virus attacks immune cells, causing acute suppression of the immune system. The World Health Organization recommends a two-dose vaccination policy, with the first dose administered during the 1st year of life, and coverage should be maintained in at least 90–95% of the population to halt transmission. In many countries, the measles vaccine is included in the immunization program and is freely available to all. Today, despite active immunization of the population, measles still occurs in the Republic of Kazakhstan.

AIM: The objective of our study was to analyze the epidemiological characteristics of measles in the Republic of Kazakhstan during the rise of the disease.

METHODS: Statistical data were obtained from the Committee on Public Health Protection on the incidence of measles in The Republic of Kazakhstan for the period from November 1, 2018 to December 30, 2019.

STUDY DESIGN: Epidemiology survey.

RESULTS: The article contains epidemiological data on the incidence of measles in the regions of the Republic of Kazakhstan among children, age, and gender characteristics.

CONCLUSION: In the period from November 2018 to December 2019, there was a tendency to increase the incidence of measles in the republic. In terms of morbidity, Nur-Sultan was the leader, where the number of cases was 22.9% (n = 3181). The largest number of registered cases, 58.2% (n = 5745), occurred in children aged 1–14 years. Measles remains an unresolved global problem and groups of undervaccinated and unvaccinated populations remain vulnerable during epidemics.

Introduction

Measles is an acutely infectious viral disease transmitted by airborne droplets (90–99% contagiousness index) and is one of the main causes of death in unvaccinated children [1], [2], [3], [4], [5], [6]. Researchers have shown that measles is most severe in young children with malnutrition, especially those with Vitamin A deficiency [7], [8], [9], [10], [11], [12] as well as in the presence of an unfavorable premorbid background [11].

The World Health Organization (WHO) recommends immunization of all susceptible individuals, both children and adults, who have no contraindications for measles immunization. Administration of two doses of the measles vaccine to all children should be the standard for all national immunization programs [13]. A measles vaccine that began in 1963 [14] led to an 80% reduction in measles mortality between 2000 and 2017 worldwide [13]. Despite significant progress in measles control, outbreaks were reported in various European countries in 2010 and 2011. For example, in the Republic of Macedonia, 908 cases were registered during this period [15], in Bulgaria, 24,364 cases were registered from 2009 to 2011 [16]. In 2016, 7 million people were infected with measles worldwide. In addition, from 2000 to 2016, the annual reported incidence of measles decreased by 87%, while global measles deaths decreased by 84 [17]. In 2017, approximately 85% of the world's children received one dose of measles vaccine, while in 2000, vaccination coverage was 72% [13]. Despite the availability of a safe and cost-effective vaccine, due to the low coverage of the population (85%) in 2017, 110,000 deaths from measles were recorded in worldwide, primarily among children under the age of 5. Before the measles vaccine was introduced in 1963, epidemics occurred approximately every 2–3 years, and 2.6 million people died of measles every year [14].

Depending on the geographical location and seasonality, the manifestations of measles can mimic the clinical picture of other viral diseases. Moreover, in

people with weakened immunity, this infection may not cause the typical symptoms of measles, which is often accompanied by severe disease outcomes, especially the development of measles pneumonia and encephalitis [18], [19], [20]. Thus, the current measles elimination targets in all countries require surveillance of every case, including laboratory confirmation of suspected cases [21].

Methods

We analyzed statistical data of the Committee for the Protection of Public Health on the incidence of measles in the Republic of Kazakhstan for the period of November 1, 2018–December 30, 2019.

Results

The introduction and spread of measles in the Republic of Kazakhstan were facilitated by the global complication of the epidemiological situation around the world, including in Europe. Measles incidence monitoring shows that in European countries, the number of measles cases reached a high level in 2018, when 83,540 cases of measles and 74 deaths from it were registered in Europe. In Serbia and North Kosovo, from October 2017 to August 2019, there were 5798 cases of measles and 15 deaths in Bosnia and Herzegovina, 1489 cases of measles were reported in 2018 and 2019, while in North Macedonia, 1948 cases were reported in 2018 and 2019, Croatia had 16 cases of 19, and Greece had 3150 cases of measles [22]. The report of the WHO announced the regions where there was an increase in measles: The regions of the East Mediterranean, Europe, and America, in areas where the elimination of measles has been declared or is close to elimination. The resurgence of measles may indicate a gap in previous vaccination strategies. According to the latest WHO-UNICEF report, only five European countries reported >95% vaccination coverage with both doses of measles vaccine; the corresponding figures in Greece for the first and second doses were 97–99% and 77–83% between 2008 and 2018. Although the epidemic was contained in Greece in 2019, there was a significant increase in other European countries in the same year, with a total of 13,460 cases. Similarly, an outbreak with 1282 cases was reported in the United States of America during 2019, a country that declared measles elimination in 2000 [23].

Figure 1 shows the total incidence of measles in the Republic of Kazakhstan from 1998 to 2019. According to the data presented, the largest increase in incidence for the entire study period is noted in 2004, during which time the indicator was 106.4% (n = 16118). In connection with the additional immunization performed in 2005–2006, a decrease in the incidence rate to 0.71% was noted in 2006.

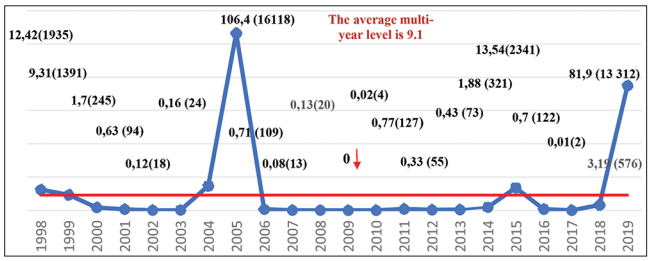

Figure 1: The long-term incidence of measles in the Republic of Kazakhstan

Epidemiological surveillance of measles in the Republic of Kazakhstan was carried out on passively registered cases and during routine surveillance. The time period from 2006 to 2014 is characterized by a period of well-being, in which the rate of registered patients ranged from 0.7% to 1%. The year 2015 was characterized by an increase in the incidence of measles, where the overall rate was 13.54% (n = 2341); against the background of increased immunization, a decrease was observed in cases from 3.1% to 0.7% between 2016 and 2018 followed by a further increase in incidence rates between 2018 and 2019 to 81.9% (n = 13,312).

Monitoring of the disease in the Republic of Kazakhstan indicates that the incidence of measles from November 2018 to December 30, 2019, amounted to 13,873 cases, of which 71.2% (n = 9875) affected children aged 6 months–14 years. In the cartogram (Figure 2), the incidence of outbreaks in four regions of the country where the number of cases exceeded 1000 patients is shown: Nur-Sultan – 22.9% (n = 3181), Shymkent – 22.3% (n = 3095), Mangistau – 10.3% (n = 1428), and in the Turkestan region – 8% (n = 1110). The following regions had a number of measles cases ranging from 200 to 1000: Atyrau, Almaty, Kyzylorda, Karaganda, Zhambyl, Akmola, Aktobe, the North Kazakhstan region, the Pavlodar region, and Almaty city; up to 200 cases of the disease were registered in Kostanay as well as in the West Kazakhstan and East Kazakhstan regions.

Most of the measles patients were young children, but all age groups, including adults, were affected to varying degrees. Since the beginning of the current measles outbreak, there is no seasonal pattern of the disease circulating all year round, with a large number of cases reported even in the summer.

The total number of measles cases in the Republic of Kazakhstan in 2018 amounted to 576 cases, of which 84% were children and 16% were adults. In 2019, the total number of measles cases increased by 23-fold compared to that in 2018 and amounted to 13,297 cases. Changes in the age structure are noteworthy, since in 2019, the number of sick children

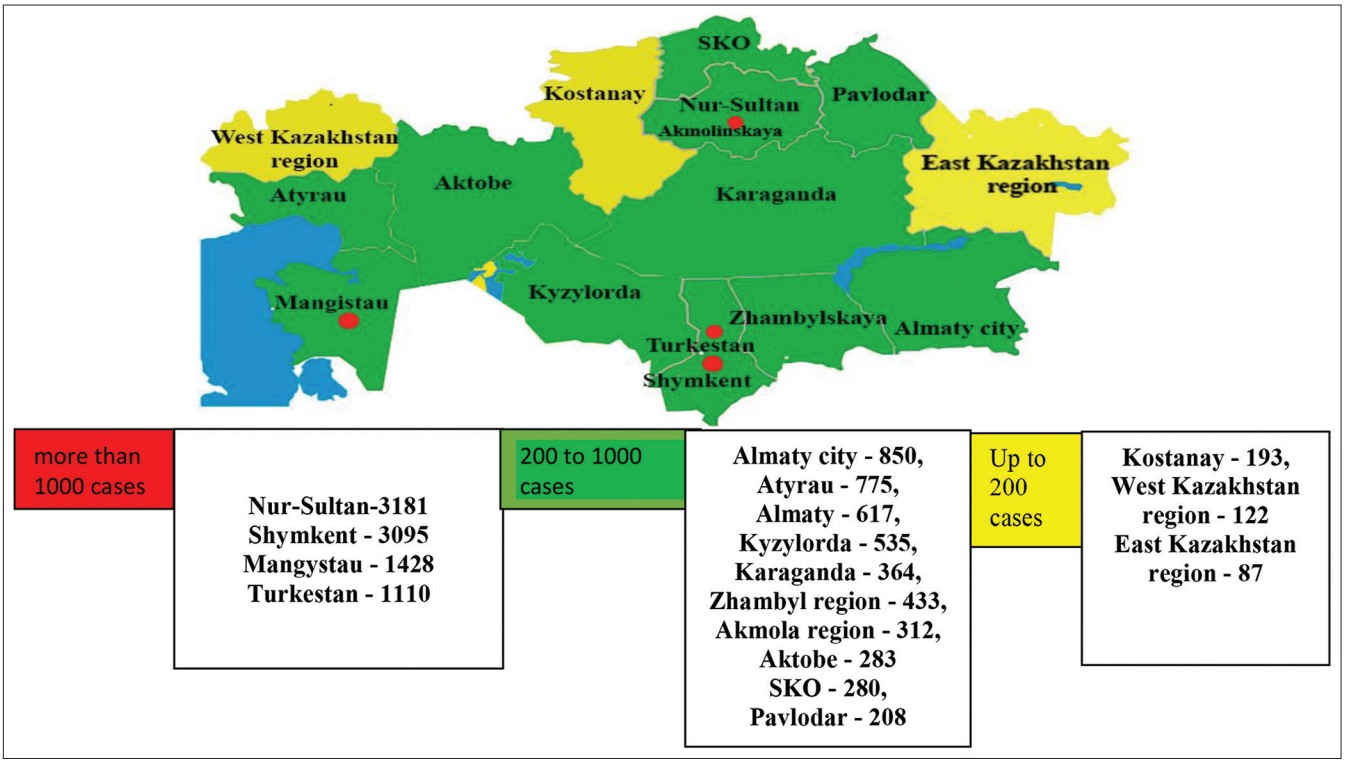

Figure 2: Monitoring of measles incidence in the Republic of Kazakhstan from November 2018 to December 30, 2019

decreased from 84% to 71%, but the incidence rates in adults increased from 16% to 29% (Figure 3).

For the regional distribution of measles incidence rates in 2018, the highest incidence in terms of the total number of cases was noted in Nur-Sultan (72.7%; n = 419), Almaty (9.7%; n = 56), Akmola Oblast (5.6%; n = 32), Turkestan Oblast (3.5%; n = 20), and Almaty Oblast (2.1%; n = 12).

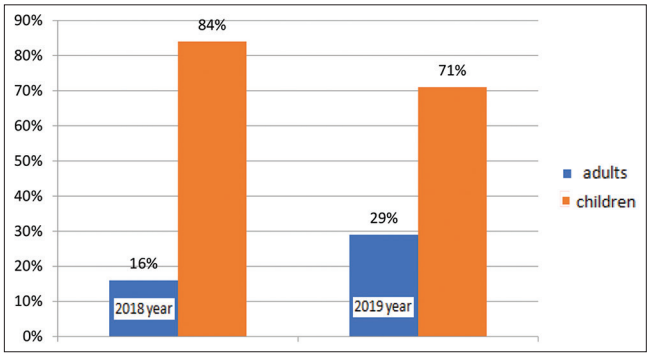

Figure 3: The incidence of measles in the Republic of Kazakhstan in 2018 and 2019

In 2019, these incidence rates, both in the regions and in the cities of Nur-Sultan and Almaty, increased significantly. For example, in the city of Nur-Sultan, the absolute indicators of the total number of cases amounted to 2762 compared to 419, that is, the number of cases increased 6.6-fold, while the relative indicators, in contrast, decreased from 73% to 20.8%. In Almaty, despite the decrease in the relative disease rates from 9.7% to 6%, the absolute number of sick patients also tended to increase, amounting to 794 versus 56, indicating an increase in the number of measles patients in the metropolis of 14.2-fold. In the Akmola region, the number of cases of the disease in absolute terms was characterized by a substantial increase to 280 from 32, which indicates an increase in the disease incidence of 8.8-fold, and there was also a tendency for the disease relative indicator to increase (5.6% vs. 2.1%) by 3.5-fold. In the Turkestan region, there was an increase in both the relative (4.7-fold; 3.5% vs. 8.2%) and absolute indicators (54.5-fold; 1090 vs. 20), which indicates an outbreak of the disease in this region. In the Zhambyl region, the increase in absolute numbers was 429 versus 4, and the relative indicator was 3.2% versus 0.7%, which indicates an increase in the relative indicator of 2.5-fold. In the North Kazakhstan region, there is an increase in the number of both absolute (279 vs. 1) and relative indicators of 1.9-fold (2.1% vs. 0.2%).

In 2019, in the Almaty region, there was a 2-fold increase in the relative incidence of measles (4.5% vs. 2.1%) and an increase in absolute indicators of 50.4-fold (605 vs. 12). In the Mangistau region, there was an increase in the absolute incidence rates of 237-fold (1422 vs. 6) and in the relative rates of 10-fold (10.8% vs. 1%). In the Karaganda region, the absolute number of measles cases increased 23.2-fold (349 vs. 15), and the relative indicator increased by 2.6%.

The following regions reported no measles cases in 2018: Atyrau, West Kazakhstan, Kostanai, and Kyzylorda; in 2019, the number of registered cases in these regions was as follows: Atyrau (5.8%; n = 775), West Kazakhstan (0.9%; n = 122), in Kostanay (1.5%; n = 193), and Kyzylorda (4%; n = 525), indicating the spread of the virus to other areas of the country.

Thus, the comparative assessment of the absolute and relative indicators of measles incidence in the country was characterized by the intensive spread of the measles virus to all regions of the Republic of Kazakhstan (Figure 4).

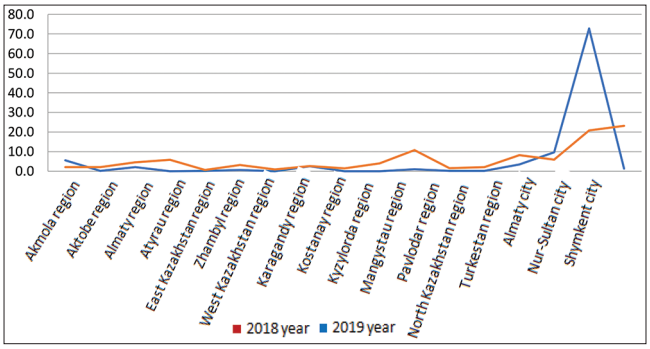

Figure 4: The incidence of measles in the regions of the Republic of Kazakhstan in 2018 and 2019

As mentioned earlier, the incidence of measles from November 2018 to December 30, 2019, resulted in 13,873 cases, of which 71.2% (n = 9875) affected children aged 6 months–14 years. Given that measles primarily occurs in children, we conducted a thorough analysis of the age and gender of children aged 6 months–1 year who were infected, since it is known that maternal immunity should be conveyed to this demographic.

The age and gender of measles patients from 0 months to 11 months. Among measles cases, children under 1 year old made up 41.8% (n = 4128) of cases. Among these, children from 0 months to 6 months amounted to 34.1% (n = 1409), children from 7 months to 8 months amounted to 28.4% (n = 1171), and children from 9 months to 11 months amounted to 37. 5% (n = 1548) (Figure 5).

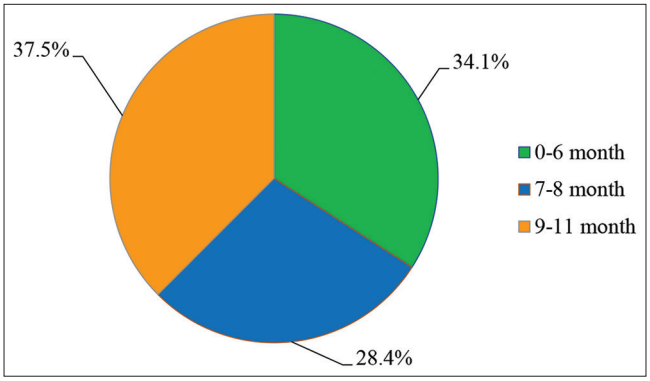

Figure 5: Age characteristics of children from 6 months to 1 year with measles in the Republic of Kazakhstan

The data obtained revealed that among infected patients, a greater number of cases occurred between the ages of 1 and 14 years, which amounted to 58.2% (n = 5745) of total cases. Among these, children aged 1 year amounted to 38.5% (n = 2213). It should be assumed that the reason for the increase in the number of children during the 1st year of life was a lack of passive immunity, since it is possible that the mothers of these children did not have measles or were not vaccinated in the late 80s or early 90s [10]. Children at 2 years old made up 18.7% (n = 1075), at 3 years old made up 12.3% (n = 708), at 4 years old made up 8.3% (n = 479), and at 5 years old made up 5.4% (n = 308) of the patient population. Notably, children undergo measles revaccination at 6 years old; accordingly, we observed that the incidence of measles decreases based on this age, so the number of sick children at 6 years old was 3.9% (n = 226), at 7 years old was 3.1% (n = 179), at 8 years old was 1.8% (n = 103), and from 10 years to 14 years was 5.9% (n = 341) (Figure 6).

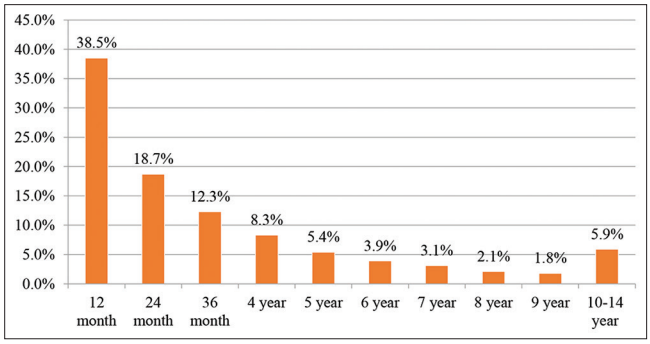

Figure 6: Age characteristics of children from 1 to 14 years with measles in the Republic of Kazakhstan

The gender of children aged 0 month–11 months who became infected with measles indicates that among children from 0 to 6 months, boys accounted for 32.2% (n = 761) of cases, and girls made up 36.7% (n = 648) of cases. At the age of 7–8 months, boys made up 28.9% (n = 684) and girls 27.6% (487) of the population. At the age of 9 months–11 months, boys made up 38.9% (n = 919) and girls – 35.7% (629) of total cases (Figure 7).

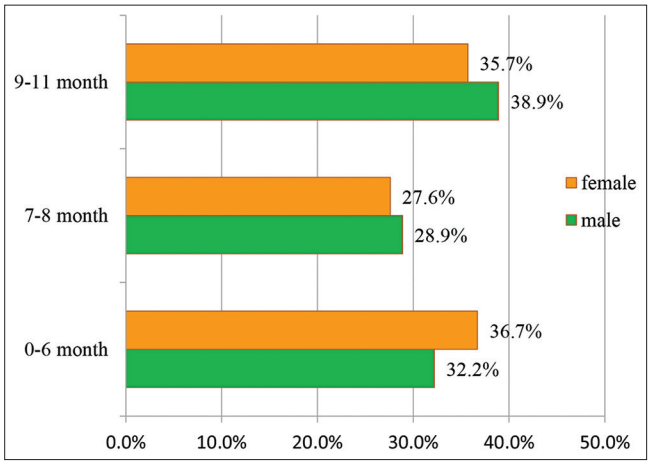

Figure 7: Gender characteristics of children from 6 months to 1 year with measles in the Republic of Kazakhstan

An analysis of gender characteristics from the age of 1–14 years showed the following results: At 1 year, boys with measles accounted for 39.9% (n = 1310) of infections and girls accounted for 36.8% (n = 903); at 2 years of age, boys comprised 18% (n = 593) of patients and girls 19.6% (n = 482); at 3 years old, boys made up 11.9% (n = 391) of cases and girls 12.9% (n = 317); at 4 years old, boys were 8.3% (n = 274) of infections and girls were 8.3% (205); at 5 years old, boys exhibited

5.3% (173) of infections and girls 5.5% (n = 135); at 6 years, boys accounted for 3.5% (n = 116) of cases and girls for 4.5% (110); at 7 years old, boys comprised 3.1% (n = 101) of cases and girls 3.2% (n = 78); at 8 years, boys made up 1.9% (n = 62) of infections and girls 2% (n = 50); at 9 years old, boys represented 1.7% (n = 57) of cases and girls 1.9% (n = 46); and from 10 to 14 years old, boys accounted for 6.4% (n = 210) of infections and girls for 5.3% (n = 131) (Figure 8). Studying the gender characteristics of children with measles, we found that male children are more susceptible to the measles virus, which confirms a the results of a previous study by the scientists Klein SL1, Marriott I2, and Fish EN3 that revealed that a higher development of antibodies to the introduced virus occurs in women compared to men. In the investigators' opinion, the development of vaccines should be gender specific to reduce adverse reactions in women and increase immunogenicity in men [24].

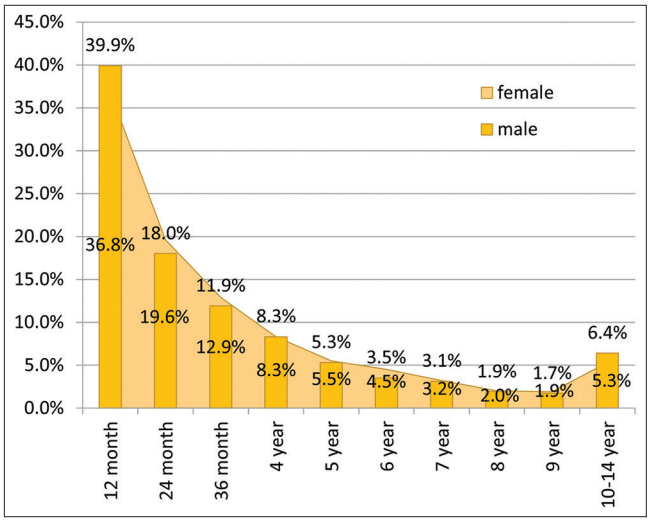

Figure 8: Gender characteristics of children from 1 to 14 years with measles in the Republic of Kazakhstan

The WHO currently considers vaccination one of the most effective and cost-effective means of fighting infections. The use of vaccines is recognized as a key element of a country's epidemic well-being [25].

To analyze the relationship between measles incidence and vaccination, we examined immunization coverage data for children with measles from November 2018 to December 2019.

The total number of sick children aged 0 month–11 months was 41.8%. We studied the vaccination coverage of these children in detail and observed that from the age of 0 month to 8 months, children did not receive the MMR vaccine, since the first dose of the vaccine is administered at 9 months, while children receive the second dose of the vaccine at 6 years old. Twenty-five children aged 9–11 months received the first dose of MMR vaccine.

The number of sick children aged 1–14 years was 58.2%. Indicator of the vaccination status of children with measles up to 1 year old did not receive the vaccine for various reasons, and children from 1 year to 14 years old were not vaccinated with the MMR vaccine in 49.8% of cases (Table 1).

Table 1: Vaccination coverage for children with measles between the ages of 0 month and 14 years

Age	Vaccination status				
	Total vaccinated, n	Of them are vaccinated		Total unvaccinated, n	%
		1-fold, n	2-fold, n		
0–6 months	0	0	0	1409	34.4
7–8 months	0	0	0	1171	28.6
9–11 months	25	25	0	1518	37.0
Up to 1 year	**25**	**25**	**0**	**4098**	**50.2**
1 year	255	255	0	1889	46.4
2 years	269	269	0	770	18.9
3 years	210	210	0	475	11.7
4 years	169	169	0	294	7.2
5 years	91	89	2	205	5.0
6 years	67	45	22	147	3.6
7 years	66	27	39	107	2.6
8 years	51	18	33	59	1.4
9 years	59	16	43	41	1.0
10–14 years	245	38	207	85	2.1
From 1 year to 14 years	1482	1136	346	4072	49.8

Measures to control the outbreak

Since April 1, 2019, an additional program of population immunization has been launched in the Republic of Kazakhstan. The vaccination program includes children who have reached the age of 9 months, persons under the age of 30 with an unknown vaccination status, those who have not previously been vaccinated and have not had measles, those who were vaccinated 5 or more years ago with a single measles vaccine in the foci of infection, as well as medical workers. Throughout the rise of the disease, health workers were offered a dose of the CCP vaccine, regardless of their immunization status or age.

To vaccinate the population, special groups were deployed for the work of the supplementary immunization program, consisting of epidemiologists and infectious disease doctors, as well as general practitioners.

To raise awareness of the population and medical professionals about the incidence of measles in the Republic of Kazakhstan, events were held among these groups. Timely information was provided on the increase in the incidence of the population and information was provided on surveillance activities and on the work of immunization through the press release of the Ministry of Health of the Republic of Kazakhstan. Information packages, including a description of measles, an update on the status of the outbreak, and a call for the population to be vaccinated, were sent to the media.

Discussion

In our study, we assessed the nature of the measles outbreak between November 2018 and December 2019. Where it was revealed that in 2019, the total number of cases of measles increased by

23 times (n = 13297) compared to 2018. The magnitude of the outbreak highlighted a significant number of susceptible children and amounted to 71.2% (n = 9875). The age structure of measles patients was dominated by children aged 1–14 years (50.2%).

Since primary vaccine inefficiency is described to occur in 2–5% of vaccinated children after the first dose of the vaccine administered at 12 months of age, the accumulation of people who did not respond to the first dose of RCT probably also contributed to the pool of susceptible children [16], [26]. It is worth noting that infected adults can transmit the measles virus to susceptible children. Moreover, susceptible mothers are unable to transmit protective antibodies against the measles virus to newborns, making them vulnerable to possible measles infection by their parents or other loved ones [27]. Our study found that more than half of the children's population in the Republic of Kazakhstan were not vaccinated or received only one dose of the MMR vaccine, which indicates that they either refused vaccination or missed various opportunities to receive the vaccine allocated by the state. During this outbreak, measles transmission occurred in several medical institutions, so cases of children with cancer were recorded. This requires clear recommendations on how to comply with infection control measures in health-care facilities and ensure that health workers and patients with background diseases are adequately protected. The measles outbreak has reminded all countries in the WHO European region of their commitments to eliminate measles. To achieve this goal, each country needs to ensure high immunization coverage (>95%) with two doses of MMR. When coverage falls below this threshold, the risk of measles outbreaks or epidemics increases exponentially [28].

The aim of this study was to investigate the clinical, gender, and age characteristics of measles during the rise in the incidence of measles among children in the Republic of Kazakhstan.

Conclusion

Measles remains an unresolved global problem, and groups of undervaccinated or unvaccinated populations remain vulnerable during epidemics. Therefore, due to the increase in the non-immune part of the population due to refusals of vaccination for various reasons, at the present stage, the levels of indicators of vaccine-controlled infections are increasing. Measles in the Republic of Kazakhstan needs further study, including the reasons for refusal of vaccination, to conduct training on the safety of vaccines and eliminate false contraindications, both among medical professionals and among the general public, to increase the level of collective immunity.

Acknowledgments

We express our gratitude to the staff of branch "Scientific and Practical Center of Sanitary and Epidemiological Expertise and Monitoring" of the National Health Service for providing reliable information on the incidence of measles among the population of the Republic of Kazakhstan.

Ethical Approval

Approval of the ethics Commission is not required, as in this study, we analyzed the incidence of measles in the population of the Republic of Kazakhstan for 2018–2019 during the rise of the disease.

Data Availability

http://www.rcrz.kz/index.php/ru/statistika-zdravookhraneniya-2.

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