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ROTAVIRAL GENOTYPE IN ACUTE INTESTINAL INFECTION IN SENTINEL SURVEILLANCE OF INFANTS FROM REPUBLIC OF MOLDOVA

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Globally, acute diarrheal disease is one of the 5 causes of death in children up to 5 years old. which was the reason for establishing the World Health Organization program to combat diarrhea at this age [1]. The World Health Organization reports the cause of death by gastrointestinal tract infections, in the European region of about 10 027 cases of deaths in children up to 5 years old. In children, 2.8 million rotaviral infections are registered annually, more than 200 deaths, with 87 000 hospitalizations in European countries [2]. Rotavirus (RV) is the most common cause of acute gastroenteritis (GEA) worldwide, affecting 95 % of children up to the age of five. Globally, RV infection is estimated to cause 3.6 million episodes of GEA per year. Until the implementation of anti-rotavirus immunization, around 2 million children with GEA of rotavirus etiology were hospitalized worldwide each year [1, 3]. By the age of 5, virtually all children have sustained rotavirus infection, this being the first cause of severe diarrhea with dehydration in infants around the world. In low-income countries, the average age of primary rotavirus infection is between 6 and 9 months (80% of cases occur in infants under one year of age), while in high-income countries the first episode sometimes occurs between 2 and 5 months (65 % of cases were seen in infants < 1 year) [4]. WHO estimates that before the occurrence of the anti-rotavirus vaccine there were approximately 453 000 deaths per year among children with rotavirus gastroenteritis (GERV) worldwide. These data accounted for approximately 5% of deaths among children, with a specific mortality rate of 86 deaths per 100 000 children < 5 years. Low-income countries from Africa and Asia are hosts for almost 90 % of the deaths caused by rotavirus thanks to the poor quality of health care [2, 4]. Implementation of sentinel surveillance of rotavirus infection in infants from the Republic of Moldova in 2008 showed a high rate of this infection (40.0 %) being an argument in recommending anti-rotavirus immunization in children within the National Immunization [5]. Program Purpose: to study the clinical-evolutionary, molecular and epidemiological aspects of rotavirus infection in infants.

Materials and Methods. The study was carried out between 2012 and 2016 and included children admitted to IMSP Municipal Children's Clinical Hospital no. 1, acute diarrheal diseases section. In the study, 193 infants with the acute diarrheal disease were monitored, under standard framework of sentinel surveillance. Depending on the vaccine status, the study sample (n = 193) was divided into group I (121 patients) - children with unvaccinated rotavirus infection and group II (72 patients) - children with vaccinated rotavirus infection. The biological material was virologically examined for rotavirus infection using the ELISA serological response and genotyping in the polymerase chain reaction (PCR). In order to confirm the rotaviral etiology of GEA, the faecal subjects of the patients in the study sample were examined. Virological investigations were carried out in the bacteriological laboratory of the National Center for Preventive Medicine in Chişinău.

Reference values: Test Specificity – 96-100 %, Test Sensitivity - 94-100 %. ELISA test detection limit: $\geq 7 \times 10^5$ viral particles per ml of the sample being investigated.

Results. From the total number of genotyped samples, the incidence of genotypes identified in patients with rotavirus infection during the preclinical period, the most common genotypes were G4P [8], G3 P [8] and G9P [8]. In the postvaccinal period, their frequency fell to the first place with the genotypes G2 P [4] and G4 P [8]. The genotypes G4, G2, G9 that cover a large proportion of rotavirus strains in the population of the country according to monitoring and sentinel surveillance data in children up to the age of 5 years (Fig. 1) are present in the vaccine used in the country.

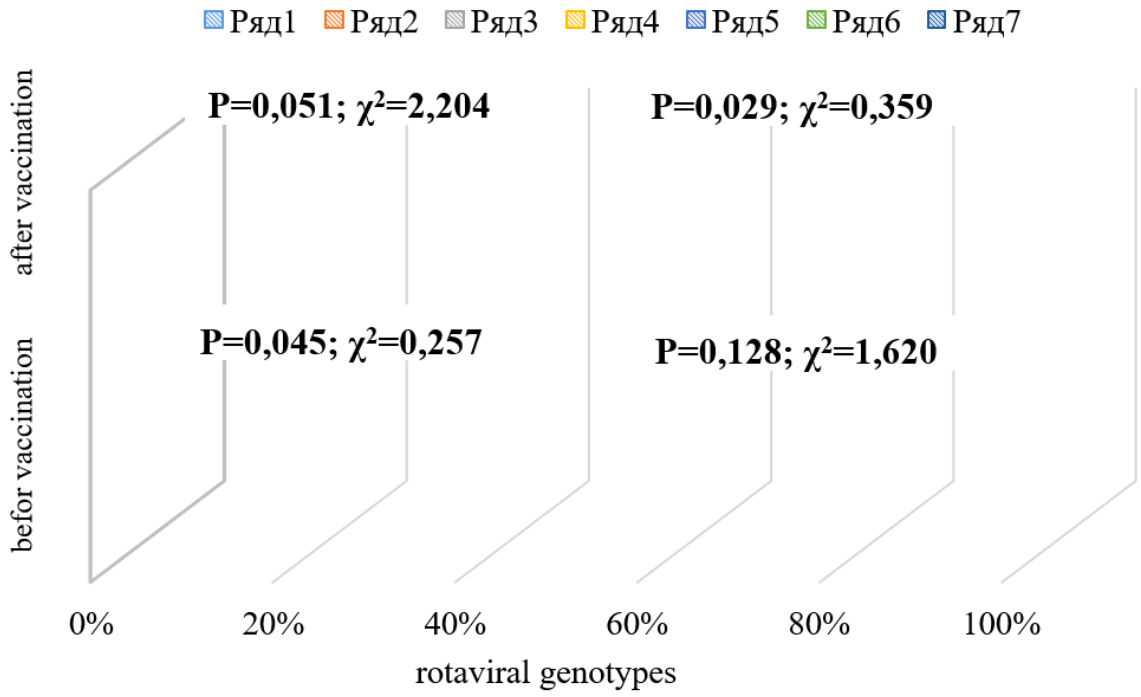

Figure 1. Distribution of genotypes before and after vaccination

The rotaviral infection is high in the cold season (January-March). Children in the study are from 1 to 12 months old, with an average age of 7.2 months. Prevalence of feminine gender (54.4 %) predominates compared to males (45.6 %). Mixed etiology - intestinal infection was predominant in the 1st study group (30.6 % children) compared to group II where the mixed share of viral infection was lower (26.4 %). Higher hospitalization duration, more severe dehydration (by 3%), the presence of severe respiratory diseases (pneumons, bronchitis, 21 %) are higher in the study group I (unvaccinated children) compared to group II vaccinated children). The bacterial infection associated with acute diarrheal disease was present in Proteus mirabilis, Klebsiella pneumoniae, Staphylococcus aureus, Escherichia coli, Proteus vulgaris, and Providencia mixofaciens.

Conclusions.

-The most common genotypes in the prevaccine period were: G9P[8], G3P[8], G4P[8] and postvaccine period: G4P[8], G2P[4]. These results demonstrate the need to continue monitoring, harvesting rotaviruses in children to strengthen control measures and respond to rotavirus infection. - Morbidity by rotavirus infection (IRV) in the Republic of Moldova decreased considerably as a consequence of the implementation of the anti-rotavirus vaccine, keeping the seasonality of the infection during the cold season of the year with an increased infestation of infants older than 6 months.

- The results of the study reconfirmed the necessity to implement the Rotarix vaccine containing genotypes G4, G2, G9 through the National Immunization Program (2012) to reduce the burden of rotavirus infection on the health system in the Republic of Moldova. - Rotavirus infection evolved as mono-infection in 67.3 % of cases and mixed-infection in 32.7 % of cases. It is associated with severe respiratory infections and pathogenic enterobacterial infections in both groups where severe clinical forms were recorded. These circumstances call for differentiated approaches in the treatment of rotavirus infection identified separately and in combination with other pathologies.

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***Key words**: children, diarrhea, rotavirus, infants.*