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ORIGINAL ARTICLE

ANALYSIS OF REGISTERED CASES OF ACUTE FLACCID PARALYSIS IN STARA ZAGORA DISTRICT AS A PART OF POLIO ERADICATION STRATEGY

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Abstract. *Poliomyelitis is the infection that, after smallpox, is a "serious candidate" for eradication worldwide. In accordance with the WHO strategy for 2022-2026, epidemiological surveillance of acute flaccid paralysis (AFP) is carried out with the aim of poliomyelitis eradication.* ***The aim*** *of the study is to determine the risk factors for the occurrence of AFP in children up to 15 years of age and to analyze the effectiveness of the established system for epidemiological surveillance of AFP, in Bulgaria.* ***Materials and methods.*** *All cases of AFP for the monitoring period 2012-2021, in Stara Zagora district, were studied. A questionnaire (34 questions) for sociodemographic and lifestyle possible risk factors for developing of AFP was also completed. Retrospective, descriptive and analytic cross-sectional epidemiological methods were applied. The data were analyzed using SPSS Statistics, Version 25.0 (IBM Corp. Armonk, NY, USA) (with Fisher's exact test).* ***Results.*** *There were 81 cases of Facial paralysis only, registered in the Web based system for surveillance of AFP, for Stara Zagora region, and 11 – AFP (without facial paralysis), for the period 2012-2021, in Stara Zagora district (92 in total). The protective factors for developing of AFP from our study were significantly associated to: having no history of paresis or paralysis in the past; absence of trauma; presence of central sewage near the home; absence of contact with animals; absence of consumption of unwashed fruits and vegetables.* ***Conclusion.*** *It is very important to carry out systematic surveillance of AFP, in children up to 15 years, with the aim of investigating all cases as part of the Global strategy for the eradication of poliomyelitis; monitoring of the immunization coverage with polio vaccine to maintain a high level; surveillance of the waste and sewage waters, twice during the year in 6 months.*

Key words: *acute flaccid paralysis, epidemiological surveillance, poliomyelitis, eradication, risk factors, protective factors*

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INTRODUCTION

Poliomyelitis is the infection that, after smallpox, is a "serious candidate" for eradication worldwide. The disease affects childhood. It is characterized by a severe course, high mortality and is the main cause of disability in children, in the pre-immunization period. Approximately 1% of cases develop paralytic poliomyelitis. In 2019 WHO announced the eradication of wild poliovirus 3, and wild poliovirus 2 was eradicated in 2015. Wild poliovirus 1 continues to circulate. Currently, WHO considers the

occurrence of even 1 confirmed case of polio as an epidemic. In the WHO Strategy 2022-2026 for eradication of poliomyelitis worldwide there are two main goals: permanently interrupt all poliovirus transmission in endemic countries, stop cVDPV (circulating vaccine-derived poliovirus) transmission and prevent outbreaks in non-endemic countries. In the last 5 years much more cases are reported from vaccine-derived polioviruses than from wild serotypes [1, 2, 3]. The causative agent of poliomyelitis is human poliovirus, which is a member of the genus Enterovirus of the Picornaviridae family. Enteroviruses spread either through the faecal-oral route or via respiratory transmission. They are transmitted by eating and drinking contaminated food and water and through contaminated hands. The entrance doors are the digestive system or nasopharynx.

The Nobel Prize in Physiology or Medicine 1954 was awarded jointly to John Enders, Thomas Weller and Frederick Robbins “for their discovery of the ability of poliomyelitis viruses to grow in cultures of various types of tissue”. This was the basis for vaccine development. In Bulgaria, the live poliomyelitis vaccine (Sabin) was introduced in 1959. According to the instructions of the European Health Commission in Bulgaria, since 2007, the inactivated vaccine (Salk) has been used within the immunization schedule of the Republic of Bulgaria [4, 5, 6]. Acute flaccid paralysis (AFP) surveillance is the gold standard for detecting cases of poliomyelitis. The detection, even in the absence of polio, of at least one case of AFP per 100,000 children under the age of 15 serves as an indicator of the sensitivity of the surveillance system [7, 8]. In 2022 cVDPV type 2 and type 3 have been found in unvaccinated patients in UK (and in the environment – in sewage samples collected from north London and east London), USA, Ukraine and Israel [9].

There are also risks in administering of the oral polio vaccine. Prolonged excretion of vaccine polioviruses is obtained in persons with immune deficiency. Wild polioviruses are potential “biological” weapons [10]. The complete sequence of the poliovirus genome was deciphered in 1981 by two research groups of Vincent Racaniello and David Baltimore of the Massachusetts Institute of Technology and Eckart Wimmer of New York [11].

Non-polio enteroviruses (NPEVs) and human parechoviruses (PeVs) are included in the established European non-polio enteroviruses Network-ENPEN, covering 17 European countries. The diseases caused by non-polio enteroviruses are: meningitis (in children and young people), myocarditis, acute flaccid paralysis, encephalitis, hand-foot-and-mouth disease, neonatal sepsis. There are no developed vaccines. EV-68 is the cause of respiratory infections and acute flaccid paralysis in 17 countries including Bulgaria [12].

Enterovirus 71 (EV71) has become a major neurological threat worldwide since the eradication of poliovirus. Most EV71 infections usually result in hand-foot-and-mouth disease (HFMD) or herpangina, and some cases are associated with brainstem encephalitis and acute flaccid paralysis [13]. The first identification of enterovirus D-68 was made in 1962, in registered respiratory diseases in the USA, in Europe and Asia, called “northern virus”, from the family Picornaviridae [14]. Enteroviruses reach the central nervous system (CNS) through neuromuscular junctions or by directly crossing the blood-brain barrier. Replication of viruses in motor neurons follows. Aseptic meningitis is caused by enteroviruses in half of the cases. Enterovirus-71 has been associated with viral meningitis and AFP and Coxsackie viruses can cause meningoencephalitis [15].

MATERIALS AND METHODS

Research methods

The aim of the study was to determine the risk factors for the occurrence of AFP in children up to 15 years of age and to analyze the effectiveness of the established system for epidemiological surveillance of AFP, in Bulgaria. AFP surveillance is the gold standard for detecting cases of poliomyelitis. It consists of four steps of observation: 1) Finding and reporting of children with AFP; 2) Transporting stool samples for analysis; 3) Isolating and identifying enterovirus (poliovirus) in the referent laboratory; 4) Mapping the virus to determine the origin of the virus strain [8].

During the study period between 2012 and 2021, all registered cases of AFP in the district of Stara Zagora were studied. Data was retrieved using the Web based system for surveillance of AFP, in the Republic of Bulgaria. Primary and secondary studies were conducted and joint control examinations with the general practitioners after 60 days of the beginning of the illness were scheduled. A questionnaire (consisting of 34 questions) for sociodemographic and lifestyle possible risk factors for developing of AFP was also completed. Retrospective, descriptive and analytic cross-sectional epidemiological methods were applied.

Statistical analyses

The data were analyzed using SPSS Statistics, Version 25.0 (IBM Corp. Armonk, NY, USA) (with Fisher’s exact test) to explore the relationship between potential factor and type of disease. Odds Ratio (OR) and

Relative Risk (RR) are similar if the prevalence of the disease is very low in relatively rare diseases [16, 17]. Relative risk (RR) with the corresponding 95% confidence interval was calculated. The assayed potential risk or protective factors for developing of AFP were: age, gender, place of residence, education, ethnicity, seasonality, previous paresis in the past, mechanical trauma, central or local water supply, availability of sewage, vaccination with live or killed vaccine, applied extraordinary dose, data on PPV of other family members, presence of residual paresis, after the 60th day, swimming in lakes, rivers, contact with animals, consumption of unwashed fruits or vegetables, timeliness of collected fecal samples, outcome of the disease, etc.

RESULTS

There were 81 cases of facial paralysis only, registered in the Web based system for surveillance of AFP, for Stara Zagora district, and 11 – AFP (without facial paralysis), for the period 2012-2021, in Stara Zagora district (92 in total) (Table 1).

Table 1. Registered cases of AFP (without facial paralysis)

Diagnosis	N of cases
Guillain-Barré syndrome	5
Encephalomyelopolyradiculoneuritis	1
Meningopolyradiculoneuritis	1
Damage to the lumbosacral plexus	1
Damage to the nervus fibularis sinistra	2
Demage to the nervus suralis dextra	1

Age distribution

All registered cases were in children up to 15 years of age in connection with the requirements of the Surveillance of AFP. The most affected were the patients aged 10-15 years – 56.5% (52 cases) (Fig. 1).

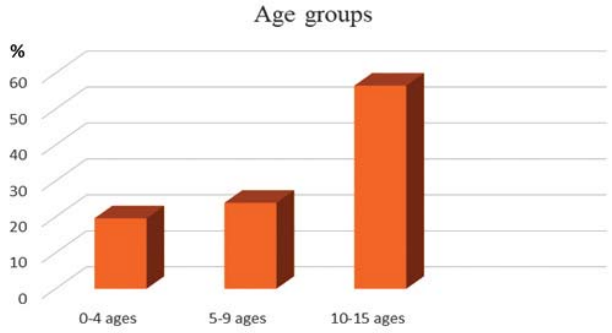


Fig. 1

A total of 71.7% (n = 66) of all registered children up to 15 years of age were students, but the remaining 28.3% (n = 26) were not attending school.

Distribution by seasonality

There was a tendency towards an even distribution of cases throughout the year (Table 2). According to Korsun from a survey undertaken in 1999-2010 the largest number of NPEVs have been isolated from June to November but the spread of poliomyelitis is year-round [18].

According to Gill et al. 90 cases of AFP have been confirmed, from January to November 2018, in the United States. Etiological agents of AFP have been enteroviruses EV-D68, EV-A71 registered during the summer-autumn season [19].

Table 2. Seasonality

Season	% (n)
Spring	23.9 (22)
Summer	28.3 (26)
Autumn	18.5 (17)
Winter	29.3 (27)
Total	100.0 (92)

Distribution by gender

Out of the 81 cases of facial paralysis, 49.4% (40) were female and 50.6% (41) were male. Out of the 11 cases of AFP without facial paralysis, 45.5% (5) were female and 54.5% (6) were male.

Distribution by place of residence

From registered patients with a diagnosis facial paralysis 29.6% (24) lived in the town Stara Zagora and 70.4% (57) – in the Stara Zagora district. Place of residence during the childhood was a town for 66.7% (54) of the cases, and for the remaining 33.3% (27) – a village.

From registered cases with a diagnosis AFP (without facial paralysis) 45.5% were living in the town Stara Zagora, 54.5% – in small towns in the district of Stara Zagora, and 18.2% – in a village.

History of paresis or paralysis

Presence of paresis or paralysis in the past have had 12.3% (n = 10) of the persons with facial paralysis. The absence of paresis or paralysis in the past was a protective factor for developing of AFP (RR 0.88; 95% CI 0.59-0.80) (Table 4).

Comorbidities

A total of 35 patients (38%) out of all 92 patients had comorbidities. It is a quite significant indicator of the pre-morbid base of occurrence of the investigated diseases (Table 3). David M. Morens et al. define the following factors as risky for AFP, the presence of

type 1 diabetes, tumors, trauma, immunopathological disorders. The transmission mechanisms are fecal-oral and respiratory. After the eradication of poliomyelitis in individual countries, the so-called "poliovirus niche" was formed. Enteroviruses have been the etiological agents of acute flaccid paralysis [1, 20].

Table 3. Comorbidities

Comorbidities	Frequency (n)	%
Ears, nose and throat diseases	5	5,43
Cold, pulmonary diseases	13	14,13
Infectious diseases	6	6,52
Diseases of the central and the Peripheral nervous system	5	5,43
Rheumatic diseases	1	1,08
Others diseases	12	13,04

Among the 35 patients with comorbidities, the frequency of ear, nose and throat diseases was 5.4% (5), rheumatic diseases – 1.1% (1), diseases of the peripheral nervous system – 4.3% (4), diseases of the central nervous system – 1.1% (1), both peripheral and central nervous system diseases – 1.1% (1).

Traumas

A total of 4.9% (4) of the patients with facial paralysis have had mechanical trauma, and the same was true for 18.2% (2) of the patients with a diagnosis of AFP (without facial paralysis). Cold trauma was found in 13.6% (11) of children with the diagnosis facial paralysis (p=0.273; RR=0.86) (Table 4).

Water supply and sewerage

All 92 patients had centralized water supply. Local water source had 1.1% (1) of all 92 patients. A total of 27.2% (25) patients did not use centralized sewage system. The presence of central sewerage was a protective factor for developing of AFP (RR 0.69; 95% CI 0.59-0.80) (Table 4).

Immunizations

According to age all patients were immunized with polio vaccine: 40.2% were covered with live vaccine, the rest – with killed vaccine – 56.5%. Three persons (3, 3%) were vaccinated with both types of vaccine according to the transition from the live to the killed vaccine (in 2007) in Immunization schedule in the Republic of Bulgaria (2 with facial paralysis and 1 with AFP, without facial paralysis).

Vaccination coverage against poliovirus has been 96.1% (in 2013), 93.4% (in 2015) in Italy which is the threshold to ensure "herd immunity". The following risk factors have been noted: low immunization coverage, migration processes, wars, social status, health system, religious positions [21]. In a study conducted in Africa the authors have concluded that mucosal immunity declines, and vaccination campaigns with type $mOPV_2$ will be required for stopping cVDPV2 transmission [22].

Control examination

About the control examination after the 60th day 73.9% (68) of people have been tested. That is almost up to the required 80% according to the WHO strategy for surveillance of AFP. Presence of residual paresis were detected in 31.9% (22) of patients with AFP.

Swimming in unregulated water sources (lakes) was detected in 3 of the cases (3.3%) with facial paralysis (81 cases).

Harmful habits of the parents

A total of 3.3% (3) of the patients' parents were consuming alcohol and 9.8% (9) have reported tobacco use.

Animals at home

A total of 32.6% (30) of the investigated patients had animals at home. The absence of paresis or paralysis in the past was a protective factor for developing of AFP (RR 0.71; 95% CI 0.55-0.91) (Table 4).

Consumption of unwashed fruits and vegetables

Consumption of unwashed fruits and vegetables was detected in 30.4% (28) of all 92 cases. The absence of consumption of unwashed fruits and vegetables was protective factor for developing of AFP (RR 0.65; 95% CI 0.60-0.77) (Table 4).

Isolates

In connection with the active surveillance of cases of AFP, all of them must be subject to virological examination. Etiologically, only two of 92 registered cases of AFP were proven through molecular diagnostics (genus Enterovirus).

According to our study, the most important route of transmission of enteroviruses is the fecal-oral route (analogous to poliomyelitis) related to social status, health habits, communal and personal hygiene. An additional route is the airborne transmission. It is associated with cold trauma in those patients registered with facial paralysis only.

Donia A et al., have reported that the wastewater monitoring system, dating back to 1989, enables an early assessment of the presence and detection of poliovirus in the environment. This is how reservoirs of wild poliovirus and vaccine-derived polioviruses could be discovered [23].

Table 4. Potential risk or protective factors for developing of AFP without facial paralysis

Factor (combined p-value)		Relative risk (RR)	CI LB	(95%) UB
Comorbidities (p = 0.065)	absence	1.80	0.81	4.00
	presence	0.54	0.32	0.93
Previous paresis or paralysis (p = 0.261)	absence	0.88	0.81	0.94
	presence	-	-	-
Trauma (p = 0.273)	absence	0.86	0.78	0.94
	presence	-	-	-
Central sewage (p = 0.024)	presence	0.69	0.59	0.80
	absence	-	-	-
Contact with animals (p = 0.069)	absence	0.71	0.55	0.91
	presence	3.94	0.59	26.11
Consumption of unwashed vegetables and fruits (p = 0.014)	absence	0.65	0.60	0.77
	presence	-	-	-

Note: The risk in bold is significant

Table 5. Potential risk or protective factors in all registered patients

Risk factors	Diagnosis		Significance of the difference of the two diseases
	Facial paralysis (0)	AFP (without facial paralysis (1)	
	% (n)	% (n)	
Comorbidities			χ^2 = 3.472; p = 0.065
Absence (0)	93.0% (53)	7.0% (4)	
Presence (1)	80.0% (28)	20.0% (7)	
Total	88.0% (81)	12.0% (11)	
Previous paresis or paralysis			χ^2 = 1.542; p = 0.261
Absence (0)	86.6% (71)	13.4% (11)	
Presence (1)	100.0% (10)	0.0% (0)	
Total	88.0% (81)	12.0% (11)	
Trauma			χ^2 = 1.474; p = 0.273
Absence (0)	88.0% (66)	12.0% (9)	
Presence (1)	100.0% (11)	-	
Total	89.5% (77)	10.5% (9)	
Central sewage			χ^2 = 4.662; p = 0.024
Presence (0)	83.6% (56)	16.4% (11)	
Absence (1)	100.0% (25)	-	
Total	88.0% (81)	12.0% (11)	
Contact with animals			χ^2 = 3.144; p = 0.069
No (0)	83.9% (52)	16.1% (10)	
Yes (1)	96.7% (29)	3.3% (1)	
Total	88.0% (81)	12.0% (11)	
Consumption of unwashed vegetables and fruits			χ^2 = 5.466; p = 0.014
No (0)	82.8% (53)	17.2% (11)	
Yes (1)	100.0% (28)	-	
Total	88.0% (81)	12.0% (11)	

DISCUSSION

The survey of the risk factors for the occurrence of AFP is important to be defined as a step towards the eradication of poliomyelitis. Our study proves the importance of the epidemiological surveillance of AFP. The main goal is to prevent a case of polio in the country.

The virological identification of AFP is of key importance for the detection of poliomyelitis cases and the deciphering of other etiological agents of acute flaccid paralysis. The mandatory character derives from the fact that no case of polio-wild or genetically modified vaccine strains should be missed. It is important to carry out systematic surveillance of AFP, in children up to 15 years, with the aim of investigating all cases as part of the Global Strategy for the eradication of poliomyelitis; timely registration of the data in Web based system for surveillance of AFP in Bulgaria; the follow-up control examinations on the 60th day from the onset of paralysis and reporting the results of the double fecal samples; monitoring of the immunization coverage with polio vaccine to achieve a high immunization coverage and compliance with the Immunization Schedule of Bulgaria [10, 11, 18].

CONCLUSION

The protective factors for development of AFP (without facial paralysis) outlined in our study were having no history of paresis or paralysis in the past; absence of trauma; presence of central sewage near the home; absence of contact with animals; absence of consumption of unwashed fruits and vegetables. The new point is monitoring of the migration flow and the immunization status of children entering the country. We propose surveillance of the waste and sewage waters, twice during the year in 6 months. New guidelines have to define for improving surveillance and collaboration between institutions, in the context of a SARS-CoV-2 pandemic and a humanitarian crisis.

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