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Outbreak of an event of unknown etiology in the municipality of El Carmen de Bolívar, Bolívar, 2014

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Title: outbreak study of an event of unknown etiology in the municipality of El Carmen de Bolívar, Colombia, 2014.

Summary

Background: The objectives of this study were to identify the demographic, social, clinical and epidemiological characteristics of the cases, establish the frequency and distribution of the events and identify the possible causal relationships between the risk factors and the events under study.

Methods: an outbreak study was carried out to epidemiologically characterize the events by reviewing medical records and HPV immunization records, active search for cases in health institutions and schools, and blood lead analysis. Attack rates and relative risks with 95% confidence intervals were calculated.

Results: 517 patients were identified, 98.4% female, 81% from urban areas.
A spread-source outbreak occurred without a common source of exposure, without sequelae, and without documented clinical or paraclinical alterations. There were only statistical differences in the presentation of nausea between vaccinated cases versus those without a vaccination record (Attack Rate Ratio 8.4 95% CI 1.17-61.19).

Conclusion: in the outbreak study, toxic and infectious etiologies and possible adverse vaccine reactions are ruled out, rethinking the approach to the problem with an analytical study of cases and controls.

KEYWORDS: outbreak, human papillomavirus.

1. BACKGROUND

On June 3, 2014, the immunopreventable team of the Public Health Surveillance and Risk Analysis Directorate of the National Institute of Health was notified of a possible outbreak of foodborne illness (ETA) due to the consumption of water or a possible event supposedly attributable to vaccination or immunization (Esavi) by the quadrivalent vaccine against human papillomavirus (HPV) that occurred on May 30, 2014, during epidemiological week 22, at the official educational institution Espíritu Santo in the municipality of El Carmen of Bolívar (Bolívar). It is reported that a group of 15 girls between the ages of 11 and 17 were treated that day in the emergency service of the ESE Hospital Nuestra Señora del Carmen in the municipality, for presenting a

clinical picture characterized by tachycardia, respiratory difficulty and paresthesia (numbness) of the hands and legs. The common history of this group of students is the consumption of bagged water and food at school, as well as the application of the second dose of the HPV vaccine during the month of March 2014.

Eight of these girls were readmitted the same day due to persistence of their symptoms, for which they were referred to clinics in Sincelejo (five adolescents) and Barranquilla (three adolescents), for specialized evaluation.

Based on the data obtained in the initial investigation, different hypotheses were proposed by the officials of the departmental health secretariat when beginning the field research work: 1. Disease transmitted by water and food-ETA (fries and water in a bag); 2. Adverse reaction to human papillomavirus vaccine; 3.

Socio-psychological phenomenon in students (use of Ouija board); 4. Reaction to pesticides (fumigation in a lot near the school) and 5. Possible poisoning by psychoactive substances.

A multidisciplinary team of professionals from the departmental health secretary of Bolívar visited the facilities of the Espíritu Santo educational institution on Saturday, May 31, without finding evidence of the use of pesticides or recent fumigation sessions. Samples of food (potato chips, packaged products, cookies®) and bagged water that are distributed in the school cafeteria were obtained, which were processed in the departmental public health laboratory (LDSP).

The microbiological analyzes of the food and water samples collected did not report the presence of microorganisms at levels higher than those allowed. On the other hand, the samples obtained from the five adolescents referred to Sincelejo for toxicological analysis of psychoactive substances did not report the presence of them.

On July 10, 2014, the Ministry of Health and Social Protection called a meeting by request of the girls' parents, due to a hypothesis that the girls were possibly being affected by the quadrivalent HPV vaccine, was strengthened in the community. At this meeting, the National Institute of Health (INS) made a commitment to the community to expand the investigation of the cases, for which technical assistance was provided to the municipality between July 15 and 18, 2014. This technical assistance included evaluated a total of 26 cases related to the event, of which 17 of the 26 girls (77.2%) with the first dose did not present any type of reaction or discomfort, two cases had pain in the arm where the vaccine was applied and two cases headache and dizziness. Regarding the application of the second dose of the biological, the girls reported the presence of expected mild reactions (induration, local pain, functional limitation, dizziness, headache, redness at the application site) with improvement between two and five days after their application. application.

During the month of July, two girls whose clinical condition persisted were evaluated in a multidisciplinary manner at the San José Children's Hospital in Bogotá, finding quantifiable levels of heavy metals (lead), for which they were diagnosed with lead poisoning.

A high-level delegation headed by the Vice Minister of Public Health and Service Provision and the director of the INS, meet with the community (parents and teachers), other authorities of the municipality and the department on August 21 to inform them that Based on the laboratory results, the case-by-case follow-up and the review of the scientific literature to date, there is no relationship between the presentation of the event of interest in public health and the application of the biological.

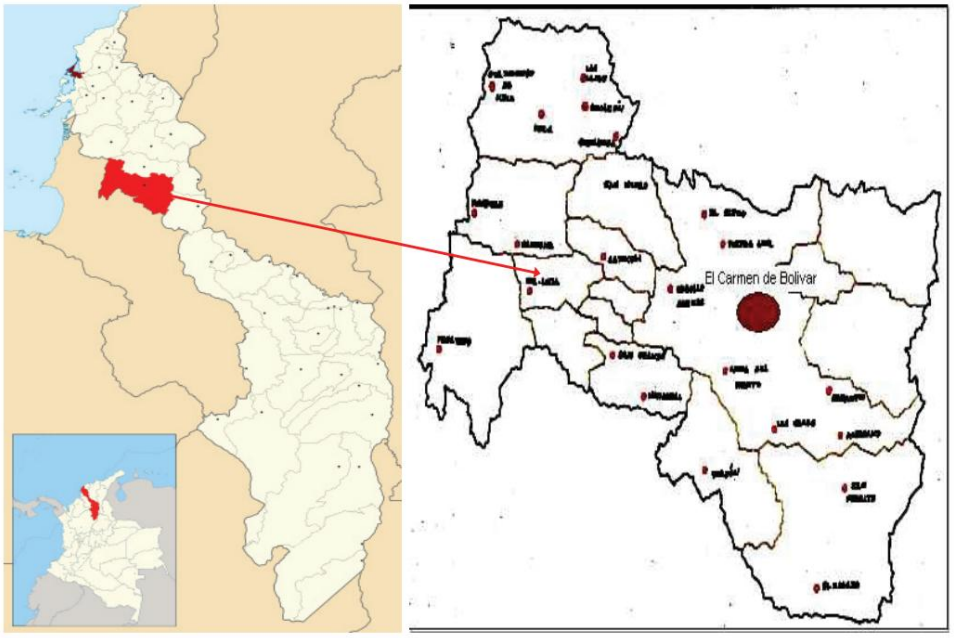
As a result of the meeting, new commitments were made with the community, among which the following stand out: specialized toxicological care in the municipality by the Ministry of Health and Social Protection, the carrying out of an epidemiological investigation by the INS, the request for support from the country's medical scientific societies to carry out a literature review on the safety of the vaccine

and the continuous monitoring of the situation presented in the municipality of El Carmen de Bolívar.

1.1 Generalities of the municipality

The municipality of El Carmen de Bolívar is located north of the department of Bolívar; It limits to the north with the municipality of San Jacinto, to the south with the municipality of Ovejas (Sucre), to the east with the municipalities of Zambrano and Córdoba and to the west with the municipalities of San Onofre and Colosó (Sucre). It has a total surface area of 954 km2, of which 45.8 km2 correspond to the municipal seat; with an altitude of 152 meters above sea level, an average temperature of 27.8ÿC, and is located 110 km from Cartagena. The fundamental basis of the economy of this municipality is agricultural activity. The municipal seat is made up of 57 neighborhoods and the rural part is made up of 19 townships distributed in three areas with 107 paths (see map 1).

Map No. 1. Geographic location of the municipality of El Carmen de Bolívar, Bolívar Colombia.



Source: Municipal Council of El Carmen de Bolivar, 2012

The municipality of El Carmen de Bolívar (according to DANE population projections for the year 2014) (1) has a population of 74,297 inhabitants, 51.7% are male (38,378) and 48.3% are male. population are women (35,919). The age groups of 10 to 14 years and 15 to 19 years make up 10.3% (7,667) of the total population of the municipality (1).

In the social aspect, situations that affect the population dynamics are described in the municipality, among which the presence of victims of violence (46%), displacement (41.8%) and families of the identification system of potential beneficiaries of social programs stand out. (Sisbén) (13.7%) (see table 1).

Table 1. Differential and preferential population of the municipality of El Carmen de Bolívar, Bolívar, Colombia, year 2011.

Population and age groups	People	Percentage (%)
Urban area inhabitants	46 656	62,8
Rural area inhabitants	25 994	34,99
Early childhood (0 to 5 years of age)	8956	12,05
Childhood (6 to 12 years old)	11 677	15,72
Pre-adolescents (13 to 15 years old)	4895	6,59
Adolescents (16 to 26 years old)	4866	6,55
Adults (27 to 59 years old)	23 038	31,01
Older adults (over 60 years of age)	7183	9,67
Children and adolescents in Families in Action	26 919	36,23
Victims of violence	34 201	46,03
Displaced by violence	31 000	41,72
Illiteracy	19 325	26,01
Family in action Sisbén 1	10 200	13,73
Economically active population	30 591	41,17
Working age population	59 780	80,46
Minor workers	5709	7,68
Afro-Colombians	668	0,9
Disabled population	225	0,3
Natives	62	0,08
LGBTI population	45	0,06

Source: municipal development plan of El Carmen de Bolívar, Bolívar, 2012-2015.

In compliance with the commitments, on August 25 and 26, an interdisciplinary team from the National Institute of Health will travel to investigate the outbreak of unknown etiology. The study was carried out with the objectives of identifying the demographic and social characteristics of the population in study, establish the frequency and distribution of the events under study, identify the clinical and epidemiological characteristics of the registered cases and establish possible causal relationships with the events under study. (Illness transmitted by water and food, poisoning with pesticides, poisoning with psychoactive substances , exposure to games with supernatural elements, possible adverse reactions to the application of the HPV vaccine and other biological agents possibly related to the mass event of unknown etiology).

2. METHODS USED IN THE FIELD

2.1. Type of study

An outbreak study was performed.

2.2. Study population

Children, adolescents and young adults residing in the municipality of El Carmen de Bolívar.

23. Case definition

Child, adolescent or young adult who consulted between May 28 and October 15, 2014 for two or more of the following symptoms: headache, paresthesias of the lower limbs, respiratory difficulty, paresthesias of the upper limbs, chest pain, fainting, from El Carmen de Bolívar.

2.4. Variables

The variables under study were sex, entity administering benefit plans, type of security, municipality of origin, neighborhood, village, telephone, date of vaccination, batch number, vaccination card, history, date of consultation, start date of symptoms, new case, paresthesia, headache, respiratory distress, nausea, vomiting, chest pain, fever, dizziness/vertigo, hyperthermia, syncope, dysesthesia, joint pain, muscle weakness, lipothymia, cough, other symptom, abnormality in physical examination, admission diagnosis, observation, medical management established, laboratories requested, referral, consultation with specialist, date of consultation, specialty, abnormality in physical examination by specialist, measurements at nominal level ; level of education, **ordinal measurement level;** age, number of doses of the vaccine received, heart rate, respiratory rate, blood pressure, pulse oximetry, evolution time, total readmissions, report of heavy metals, **measures at the ratio level.**

2.5. Data collection plan

To characterize the outbreak of the event of interest in public health of unusual frequency and etiology under investigation that occurred in children and adolescents in the municipality of El Carmen de Bolívar, the following activities were carried out:

2.5.1. Review of the initial investigation report of the Bolívar health secretary

The activities carried out up to that moment by the Departmental Health Secretariat of Bolívar are reviewed. In this process, information is provided on the consultation of a male patient from the same institution and with the same symptoms.

2.5.2. Review of medical records

A review was carried out of the medical records in physical and electronic format of the patients treated daily at the ESE Hospital of Nuestra Señora del Carmen, as well as the specialized assessment sheet carried out by the toxicology group.

clinic of the Hospital San José de Bogotá and the national notification form from Esavi to Sivigila. A database was designed in which information on the variables was captured for the characterization of the event. On the other hand, an interview was conducted with health personnel (emergency doctors and pediatricians) who have attended to the cases in health institutions to classify their clinical picture.

To verify the history of vaccination against the human papillomavirus, different sources of information were used: photocopies of the card in the medical records, verification of the card carried out in previous epidemiological field investigations and cross-checks of different identification variables of the patients. cases (identity document, full name and age) with human papillomavirus vaccination records.

2.5.3. Institutional active retrospective case search (BAI)

An active retrospective institutional search was carried out for the period from January 1 to August 31, 2014 of the cases treated in the primary data generating units (UPGD) of the municipality that are characterized in Sivigila. From the individual service provision records (RIPS), suspected cases with diagnoses related to the case definition were identified by searching for codes from the International Classification of Diseases, Tenth Revision (ICD-10). The BAI was carried out with the Sianiesp program (Information System to Support the Notification and Investigation of Events in Public Health of the INS). This information was provided in its entirety by the Saludcoop IPS Corporation of Carmen de Bolívar and by the ESE Hospital Nuestra Señora del Carmen.

After the selection of the suspected RIPS cases, their physical and electronic medical records were reviewed and those that met the case definition were classified to be included in the database.

2.5.4. Active search for cases in schools

Based on the Information System of Students Enrolled in the municipality (Simit), the census of the municipality's educational institutions located in both urban and rural areas was obtained. Based on this census, an active search was carried out in the schools for girls who, having presented the event, but did not consult a health institution. Two information capture instruments were applied: a format for capturing information on basic sanitation conditions and the state of school food services, and an individual format for identifying cases related to the event. The collected data was consolidated into a data matrix in Excel for subsequent analysis.

2.5.5. Obtaining biological samples for analysis of lead levels in blood

To determine lead in blood, whole blood samples were taken from the patients who consulted between August 22 and 27, 2014 at the ESE Hospital Nuestra Señora del Carmen with symptoms related to the event and some of their relatives (parents), prior informed consent. The samples were sent to the environmental health laboratory of the National Institute of Health for the determination of lead levels by atomic absorption spectrophotometry.

2.5.6. Diagnosis of the health and basic sanitation situation of the municipality

A field visit for environmental recognition was carried out as well as a review of official documents to identify possible environmental risk factors in public health. The physicochemical and microbiological analyzes carried out by the aqueduct company of El Carmen de Bolívar (Acuecar) were compiled with their respective drinking water quality risk index (IRCA), for the liquid it has supplied during the period from January to August. of 2014 and which was reported to the Drinking Water Quality Surveillance System (Sivicap) of the National Institute of Health.

2.5.7. Review and analysis of the municipal record of vaccination days against the human papillomavirus (HPV) carried out during the years 2012 to 2014.

Verification of the status of human papillomavirus vaccination records was carried out from 2012 to 2014, which were in physical media. Vaccination lists were consolidated digitally in Excel sheets. Among the variables that make up these records are identification data of the vaccinated girls, number of doses, dates of immunization and batches applied, and educational institution to which they belonged.

2.5.8. Analysis Plan.

The data obtained in the surveys were entered into a database whose access is restricted only to people directly involved in the study. The analysis of the information was carried out in the EpiInfo 7 ® program.

The database was refined taking into account complete completion of the survey and compliance with case criteria. Once the database had been cleaned, a general description of the variables was carried out, calculating measures of central tendency and dispersion for continuous variables and proportions for nominal data.

For the analysis of the variables according to the case definition, “odds ratio” and 95% confidence intervals were calculated.

3. ETHICAL ASPECTS

A study was carried out with minimal risk in accordance with Resolution 08430 of 1993. Informed consent was prepared for every person who agreed to obtain biological samples for lead analysis. The confidentiality of the information and the people who participated in the study was guaranteed.

4. RESULTS

41. Description of the reference population

The student population enrolled in the municipality of El Carmen de Bolívar is made up of 17,885 individuals, 52% (9,295) are men and 48% (8,590) are women.

4.2. Initial outbreak characterization

4.2.1 Food consumption

In the field research carried out by the Departmental Secretary of Health of Bolívar in the Espíritu Santo Educational Institution, in the interview with the academic coordinator and the students, allowed us to verify that food consumption within the institution was not common among the students. On the other hand, they also carried out microbiological analyzes on the food samples (plain potatoes, curly potatoes, fried maxi, bacon, donuts, BBQ potatoes, cookies®) that were consumed by the students of the initial cluster of cases of the event, which were not They presented pathogenic microorganisms (see table 2).

Table 2. Results of samples of sweets sold at the kiosk of the Espíritu Santo Educational Institution, El Carmen de Bolívar, Bolívar, 2014

Analysis carried out	Results	Reference values	Methodology used
Mesophilic CFU/g/ml	Less than 1000	10 000	plate count
Total coliforms CFU/g/ml	Less than 10	Under 3	plate count
Fecal coliforms CFU/g/ml	Less than 10	Under 3	plate count
Staphylococcus aureus coagulase positive	Less than 100	Less than 100	plate count
Molds and Yeasts CFU /g/ml	Less than 100	100-300	plate count

Source: Departmental Laboratory of Public Health, Bolívar.

Bag water samples were collected for microbiological analysis, which were negative (see table 3).

Table 3. Results of bagged water samples analyzed at the Espíritu Santo Educational Institution, El Carmen de Bolívar, Bolívar, 2014

Analysis carried out	Results	Reference values	Methodology used
Total coliforms CFU/g/ml	Less than 10	Under 3	plate count
Fecal Coliforms CFU/g/ml	Less than 10	Under 3	plate count

Source: Departmental Laboratory of Public Health, Bolívar.

4.2.2. Consumption of psychoactive substances

No quantifiable levels of psychoactive substances (benzodiazepines, barbiturates, cannabinoids, amphetamines) were documented in the six cases of the initial cluster that were referred to more complex institutions in the city of Sincelejo for specialized management.

4.2.3. Exposure to games with supernatural elements

The practice of games with supernatural elements was not documented in the interviews carried out with teachers, girls or parents, particularly due to the community's rejection of the topic.

4.3. Characterization of the outbreak (person, time and place)

Based on the patient care records of the Nuestra Señora de El Carmen ESE of the municipality, from the date of the beginning of the outbreak (May 29) until October 15, the review of the 629 medical records of patients treated in the emergency service with a clinical picture compatible with the event under study.
112 patients who did not meet the case definition criteria were excluded (because they presented a symptom or were not from the municipality of El Carmen de Bolívar). As a result of said review 517 patients were identified who met the case definition criteria.

4.3.1. Characterization of the event in person

Of the 517 cases, 98.4% are female, with an average age of 14.2 years; The age group between 13 and 15 years old has the highest percentage of cases with 50.1%. 89.4% belong to the subsidized social health security regime and the vast majority are affiliated with the health benefits plan management company, Mutual Ser (see table 4).

Table 4. Distribution of cases of the event of unknown etiology by age group, social security affiliation regime and company that administers health benefit plans, El Carmen de Bolívar, Bolívar, 2014.

Characteristics		Number of cases	Percentage (%)
Age group	5 a 8	3	0,6
	9 a 12	105	20,3
	13 a 15	259	50,1
	16 a 19	147	28,4
	20 a 22	3	0,6
Social security scheme	Subsidized	462	89,4
	Contributory	33	6,4
	Special	14	2,7
	Uninsured	5	1
	Exception	2	0,4
	Since given	1	0,2
Benefit plan administration company	Mutual ser	307	59,4
	Ambuq	69	13,3
	Healthcoop	30	5,8
	Cajacopi	24	4,6
	Coosalu	22	4,3
	Others	59	11,4
	Uninsured	5	1
	Since given	1	0,2

Source: Case database, field research team, National Institute of Health.

According to the educational institution to which the cases belong, 57.7% (293) study in five educational institutions: Espíritu Santo (75), Gabriel García Taboada (67), Maria Immaculada (55), Manuel Edmundo Mendoza (48) and the Caracoli Educational Institution (48) (see Table 5).

Table 5. Distribution of cases by educational institution, El Carmen de Bolívar, Bolívar, 2014.

Educational institution	Number of cases	Percentage (%)
Holy Spirit	75	14,5
Gabriel Garcia Taboada	67	13
Mary Immaculate	55	10,6
Manuel Edmundo Mendoza	48	9,3
Caracolí Educational Institution	48	9,3
Agricultural Technician Geovanny Cristini Cristini	42	8,1
Industrial Technician Juan Federico Hollman	34	6,6
Mammon of Mary	30	5,8
Gabriela Mistral	28	5,4
Agricultural Technician Julio Cesar Turbay	25	4,8
Social Promotion Technician	13	2,5
Ecological Technician Emma Cecilia Arnold	11	2,1
The Hobo	9	1,7
Antonio Ricaurte	8	1,5
High mountain	4	0,8
San Rafael	3	0,6
The salty	1	0,2
Since given	16	3,1
Total	517	100

Source: Case database, field research team, National Institute of Health.

4.3.2. Characterization of the event in place

Of the total cases, 81% (419) come from the urban area, 19% (98) of the cases reside mainly in the Los Laureles, Los Mangos, Ocho de Junio, Siete de Agosto and El Vergel neighborhoods (see table 6).

Table 6. Distribution of cases from the urban area by neighborhood of residence, El Carmen de Bolívar, Bolívar, 2014

Residence neighborhood	Number of cases	Percentage (%)
The laurels	33	6,4
The Mangos	28	5,4
June 8th	22	4,3
August seventh	18	3,5
The Orchard	16	3,1
Minute of God	15	2,9
New town	15	2,9
Bureche	14	2,7
The Concord	14	2,7
The Wasteland	13	2,5
Jorge Elicer Gaitán	13	2,5
The meadow	12	2,3
The colonies	11	2,1
Flowers	11	2,1
Mount Carmel	11	2,1
Ceiba	10	1,9
The Forest	10	1,9
Nariño	10	1,9
Other neighborhoods	127	25
Since given	16	3,1
Total	419	81,3

Source: Case database, field research team, National Institute of Health.

Regarding the cases residing in the rural area, 6.2% come from the Caracolí district, 4.8% from Loma Central and 1.2% from El Hobo (see table 7).

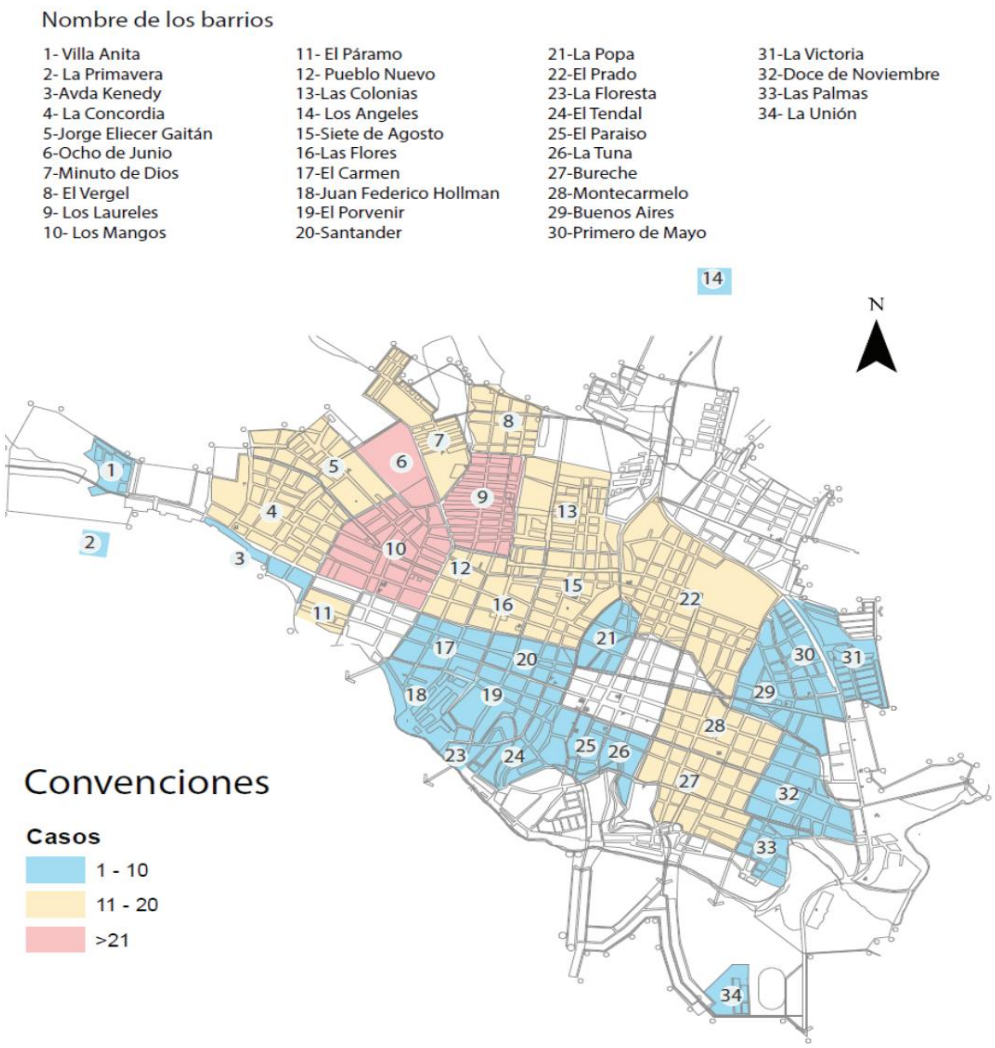
Table 7. Distribution of cases from rural areas by area of residence, El Carmen de Bolívar, Bolívar, 2014

Residence sidewalk	Number of cases	Percentage (%)
Snail	32	6,2
Loma Central	25	4,8
The Hobo	6	1,2
Don Cleto	4	0,8
Alferez	3	0,6
Beautiful	3	0,6
Shrimp	3	0,6
Coloncito	2	0,4
The Bledo	2	0,4
La Cansona	2	0,4
Lorraine	2	0,4
Mammon of Mary	2	0,4
Saint Anthony	2	0,4
Other trails	10	2
Total	98	19

Source: Case database, field research team, National Institute of Health.

When georeferencing the cases registered by neighborhood of residence, these are concentrated in the neighborhoods located in the northwestern area of the municipality such as Los Laureles, Los Mangos, Ocho de Junio, Siete de Agosto and El Vergel (areas in green) (see map 2).

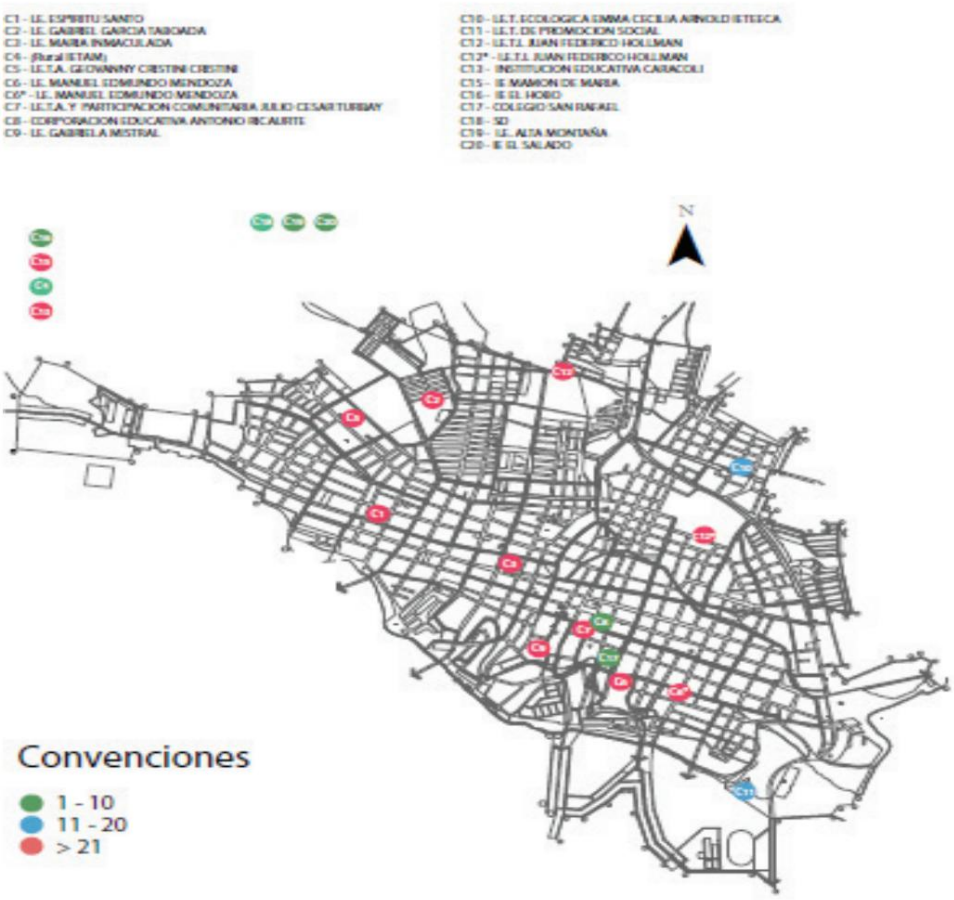
Map No. 2. Cases registered in the urban area and neighborhood of residence, El Carmen de Bolívar, Bolívar, 2014.



Source: Consolidated Case Database, Field Research Team, National Institute of Health.

By educational institution, similarly the highest frequency of cases are found in educational institutions located in the northwestern area of the municipality such as Espíritu Santo educational institution, Geovanni Cristinni educational institution and Gabriel García Taboada educational institution (see map 3).

Map No. 3. Cases by educational institution in the urban area, El Carmen de Bolívar, Bolívar, 2014



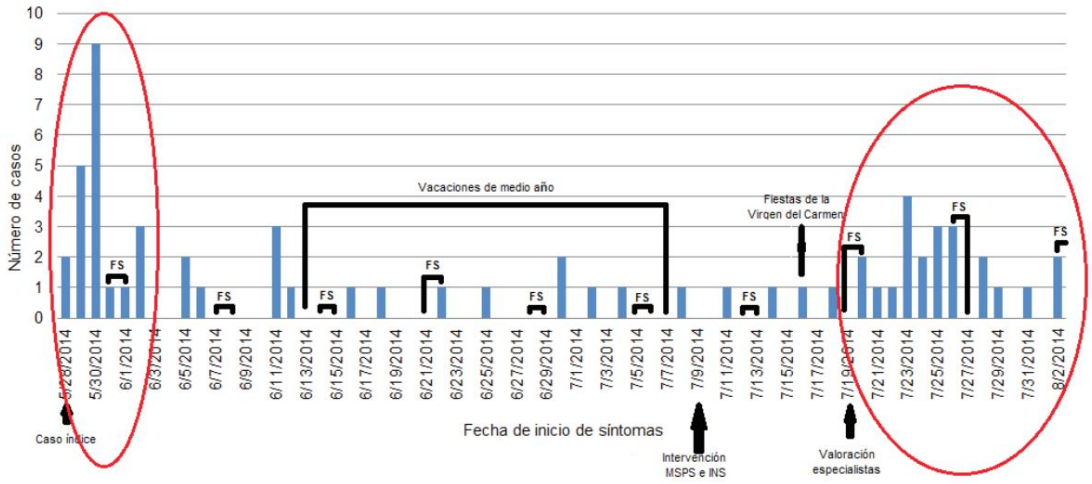
Source: Consolidated Case Database, Field Research Team, National Institute of Health.

4.3.3. Characterization of the event in time

Four time periods with a greater frequency of case presentation are highlighted. The appearance of the index case was on May 28, 2014, with subsequent occurrence of the 15 cases of the first cluster notified to Sivigila in epidemiological week 22.

(May 25-31) with decline in the following week. Then a second increase in cases is recorded in epidemiological weeks 30 and 31, mainly on July 23 (four cases). Of the ten weekends included during these two time periods, four had cases (see figure 1).

Figure No. 1. Epidemic curve of the outbreak of the unusual event and unknown etiology, El Carmen de Bolívar, Bolívar, epidemiological weeks 22 to 31 of 2014

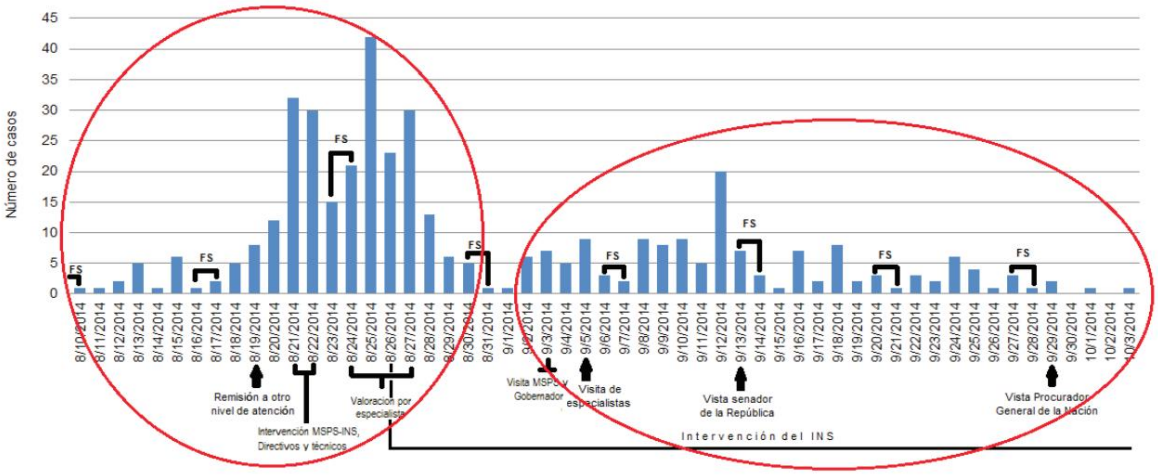


Source: consolidated case database, field investigation team, INS.
FS: weekend

During epidemiological weeks 33 to 35 (August 10 to 30), another episode occurs, with day 24 being the day with the highest number of cases; During this time interval, four weekends were spent, of which only an increase is shown on August 24. The next case submission period

It goes from epidemiological week 36 to 40, with great importance on September 12. Cases decrease noticeably during week 41 (week of recess for educational institutions), registering one case every other day; During this period there are four weekends with case registration (see figure 2).

Figure No. 2. Epidemic curve of the outbreak of the unusual event and unknown etiology, El Carmen de Bolívar, Bolívar, epidemiological weeks 33 to 40 of 2014

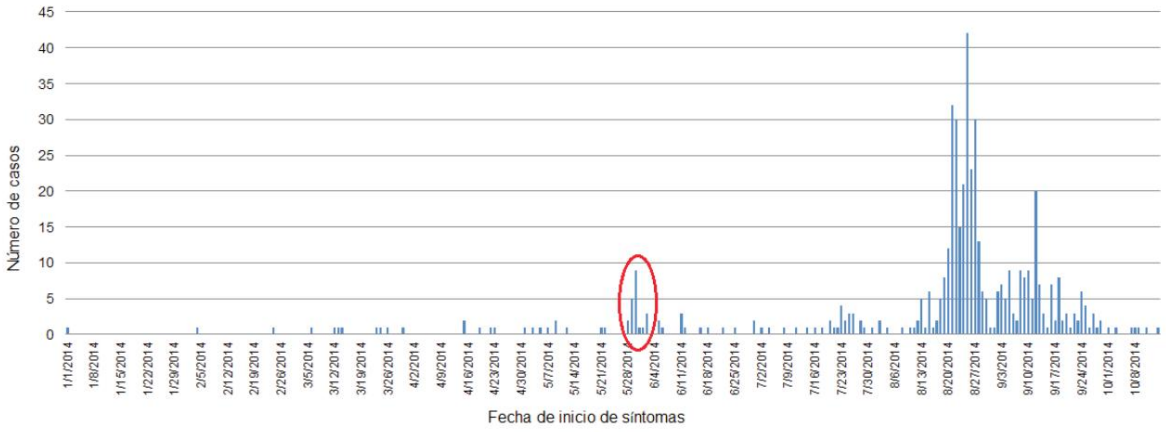


Source: consolidated case database, field investigation team, INS. FS: weekend

According to the behavior described above, the epidemic curve of the event can be classified as having a propagated source, given the progressive increase in the appearance of cases in intercalated time periods (waves) of their presentation.

On the other hand, when configuring an epidemic curve with the epidemiological weeks prior to the notification of the initial cluster (red circle) with the cases captured in the active institutional search, 25 cases are found with onset of symptoms since January 1, 2014 (see figure 3).

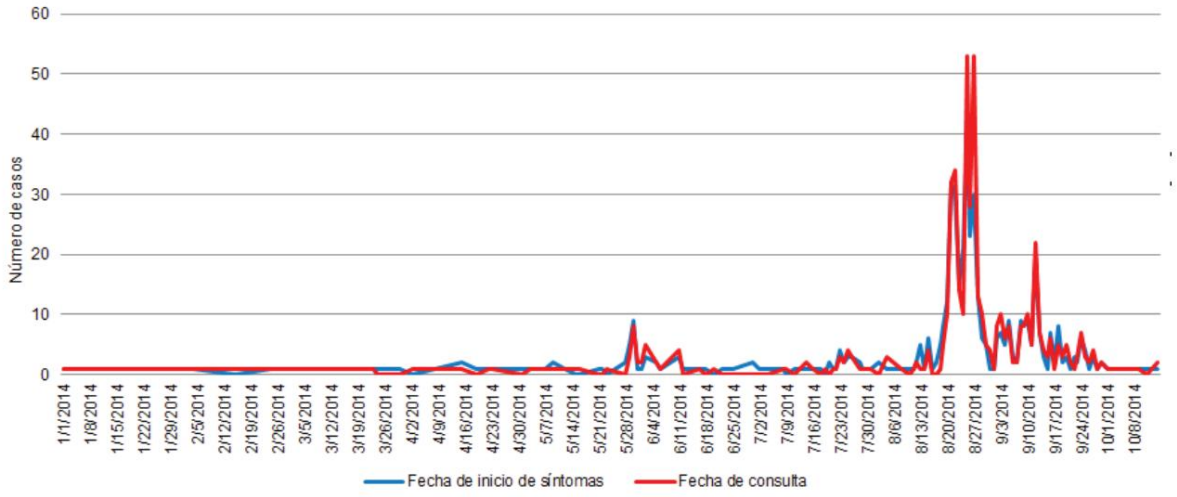
Figure No. 3. Epidemic curve of cases of unusual event and unknown etiology in active institutional search, El Carmen de Bolívar, Bolívar, 2014



Source: consolidated case database, field research team, INS.

The above shows the behavior of the event taking into account the date of onset of symptoms, however the date of consultation is relevant, since many of the patients consulted the health services several times, dates that are not necessarily dates of occurrence of the event. cases but recidivism of the patients (see figure 4).

Figure No. 4. Comparison of the behavior of the event of unknown etiology between the date of onset of symptoms and the patients' consultation, El Carmen de Bolívar, Bolívar, 2014



Source: consolidated case database, field investigation team, INS

When georeferencing the frequency of presentation of cases of the event of unknown etiology by month of onset of symptoms, in the months of May and June these are concentrated in the neighborhoods located in the northwestern area of the municipality such as Los laureles, Los mangoes, Minute of
Dios, Pueblo Nuevo and La Concordia, as well as in the southeastern area of the municipality in the Doce neighborhoods of November (blue areas). In the month of July, the cases occurred towards the center of the municipality in the El Carmen, La Popa, El Paraíso and Monte Carmelo neighborhoods (green areas). Finally, in the month of August and September, the cases occurred in the rest of the municipality, without a pattern of geographical dispersion of them (purple areas and stars) (see figure 5).

Map No. 5. Cases in the urban area by month of onset of symptoms, El Carmen de Bolívar, Bolívar, 2014.

Source: Consolidated Case Database, Field Research Team, National Institute of Health

In the month of August, the frequency of the onset of symptoms in students skyrockets in almost all of the schools in the municipality, both in urban and rural areas, a trend that continues in the month. month of September. This distribution of cases by schools shows a random pattern in their appearance, without determining a particular dispersion of cases that is associated with a common source of exposure.

4.3.4. Characterization of the event according to clinical aspects

4.3.4.1 Immunization history: the review of the records documented that 76.9% (398) of the cases received at least one dose of the vaccine. HPV vaccine, 65.2% (337) two doses and 5% (26) three doses. In 3.9% (20) of the cases, the existence of a vaccination card is reported (see table 8).

Table 8. Consolidated VHP vaccine doses by case, period and batch applied, municipality of El Carmen de Bolívar, Bolívar, 2014.

HPV vaccine dose	Frequency	Percentage (%)	Number and reference of lots
1	398	76,9	4: H012514, J004440, J004479 y J005613
2	339	65,5	4: H012514, J004479, J005213 y J005613
3	26	5,1	2: H020044,J004479

Source: Case database, field research team, National Institute of Health.

4.3.4.2 Medical history: In 8.3% (44) of the cases, some significant pathological medical history was reported in the clinical history. Of this group of cases, the 11 individuals with a history of similar clinical symptoms prior to the outbreak stand out. Seven of these presented their symptoms between three to 16 months prior to the first dose administered against HPV. Similarly, six cases with a psychiatric history were documented: four with a history of suicide attempts, one with a history of probable sexual abuse and one case with a history of depression (see table 9):

Table 9. Significant medical history of the event cases of interest in the study according to school, municipality of El Carmen de Bolívar, Bolívar, 2014.

Relevant medical history	Frequency	Percentage (%)
No background	473	91,5
Similar pictures prior to the outbreak	11	2,1
Neurological pathologies (migraine, epilepsy)	8	1,5
Cardiopulmonary pathologies (asthma, heart disease under study)	7	1,3
Family members (diabetes, depression)	6	1,1
Psychiatric pathologies (depression, suicide attempt, suspected sexual abuse)	6	1,1
Environmental exposure (mechanical shop)	3	0,6
Autoimmune pathologies (systemic lupus erythematosus)	1	0,2
Surgical (congenital heart disease correction)	1	0,2
Metabolic pathologies (hypoglycemia)	1	0,2

Source: Case database, field research team, National Institute of Health.

4.3.4.3 Presence of symptoms: A higher percentage was reported as having an acute presentation with a period of evolution between a few minutes and 14 hours in 52.4% (271) of the cases (see table 10). According to

Table 10. Evolution time between the onset of symptoms and the consultation according to the report in the medical history for the cases of the event of interest in the study according to school, municipality of El Carmen de Bolívar, Bolívar, 2014.

Time of evolution of reported symptoms	Frequency	Percentage (%)	range evolution
Minutes	135	26,1	1 to 45 minutes
Hour	136	26,3	1 to 14 hours
Days	167	32,3	1 to 30 days
Months	17	3,5	1 to 12 months
Since given	61	11	

Source: case database, field research team, National Institute of Health.

Frequency of presentation of clinical symptoms reported by the cases, headache (80.1%), paresthesias in lower limbs (60.4%) and paresthesias in upper limbs (46.2%) were the most frequent (see table 11). .

Table 11. Frequency of symptoms reported by the cases of the event of interest in the study according to school, municipality of El Carmen de Bolívar, Bolívar, 2014.

Symptom	Frequency	Percentage (%)
Headache	414	80,1
Lower limb paresthesias	312	60,4
Upper limb paresthesias	239	46,2
Chest pain	216	41,8
Dizziness/vertigo	148	28,6
Syncope	125	24,2
Respiratory difficulty	105	20,3
Muscular weakness	78	15,1
Perioral paresthesias	49	9,5
Nausea	33	6,4
Joint pain	31	6
Threw up	23	4,5
Fever	12	2,3
fasciculations	11	2,3
Hyperthermia	2	0,6

Source: Case database, field research team, National Institute of Health.

Regarding the most frequent combinations of symptoms that characterize the clinical picture, there are headaches associated with paresthesias in the upper and lower extremities or headaches associated with a feeling of dizziness (see table 12).

Table 12. Frequency of symptoms reported by the cases of the event of interest in the study according to school, municipality of El Carmen de Bolívar, Bolívar, 2014.

Symptom	n (%)
Headache + Paresthesias in lower limbs + Paresthesias in upper limbs	26 5
Headache + Dizziness/vertigo	23 4,4
Headache + Paresthesias in lower limbs + Paresthesias in upper limbs + Syncope	20 3,9
Headache + Paresthesias in lower limbs + Paresthesias in upper limbs + Chest pain	19 3,7
Headache + Paresthesias in lower limbs	15 2,9
Headache + Chest pain	11 2,1
Headache + Paresthesia in lower limbs + Chest pain	10 1,9
Headache + Paresthesias in lower limbs + Paresthesias in upper limbs + Dizziness/vertigo	9 1,7
Headache + Syncope	8 1,5
Headache + Chest pain + Respiratory difficulty	7 1,4
Chest pain + Respiratory difficulty	7 1,4
Headache + Paresthesias in lower limbs + Paresthesias in upper limbs + Respiratory difficulty	6 1,2
Headache + Chest pain + Lipothymia	6 1,2
Headache + Paresthesia in lower limbs + Respiratory difficulty	6 1,2
Dizziness/vertigo + Lipothymia	6 1,2
Paresthesias in lower limbs + Paresthesias in upper limbs	6 1,2
Headache + Chest pain + Dizziness/vertigo	5 1
Headache + Dizziness/vertigo + Muscle weakness	5 1
Headache + Paresthesia in lower limbs + Lipothymia	5 1
Headache + Paresthesias in lower limbs + Paresthesias in upper limbs + Lipothymia	4 0,8
Paresthesias in lower limbs + Paresthesias in upper limbs + Chest pain + Perioral paresthesia	4 0,8
Cephalea + Lipodymia	4 0,8

Source: Case database, field research team, National Institute of Health.

4.3.4.4 Findings on physical examination: The vital signs obtained from the clinical histories of the cases of the event, report in their highest percentage values within the normal range for age. The increase in respiratory rate (tachypnea) and heart rate (tachycardia) were the main alterations in the vital signs of the cases upon admission (see table 13):

Table 13. Alterations in the vital signs of the cases attended by an event of interest in public health, municipality of El Carmen de Bolívar, Bolívar, 2014.

Vital sign/Reference values	Reference values n (%) (60 to	Abnormal values n (%) (>100)	Sin given n (%)
Heart rate (beats/minute)	**100)** 496		
	(95.9) **(12 to**	9 (1,7)	12 (2,3)
Respiratory rate (breaths/minute)	**22)**	**(>22)**	
	471 (91,1)	29 (5,6)	17 (3,2)
Systolic blood pressure (mm Hg)	**(>90)**	**(<90)**	
	440 (85,1)	6 (1,1)	71 (13,7)
Diastolic blood pressure (mm Hg)	**(>60)**	**(<60)**	
	444 (86)	2 (0,2)	71 (13,7)
Temperature (°C)	**(36,5 a 37,5)**	**(ÿ38)**	
	369 (71,3)	9 (1,7)	139 (26,8)
Glasgow neurological scale score	**(15)**	**(<15)**	
	445 (80,4)	0 (0)	72 (13,9)
Oxygen saturation (%)	**(ÿ90)**	**(<90)**	
	5 (0,9)	0 (0)	512 (99,1)

Source: Case database, field research team, National Institute of Health.

In what was reported in the physical examination on admission, in 12.2% (62) of the cases, some relevant clinical finding was described without describing the presence of signs of neurological deficits in the state of consciousness, sensory or focal motor in some of them. them (see table 14).

Table 14. Main findings reported from the physical examination of the cases attended event of interest in public health, municipality of El Carmen de Bolívar, Bolívar, 2014.

Positive findings on physical examination	Frequency	Percentage (%)
Agitation and/or anxiety and/or painful facies	24	4,6
Pain on palpation of rib cage	7	1,4
Abdominal palpation pain	4	0,8
Cervical palpation pain	4	0,8
Mucocutaneous pallor	3	0,6
Positive percussion fist	2	0,4
Auscultable heart murmur Pregnant	2	0,4
uterus	2	0,4
Wheezing	1	0,2
Pain on palpation in knee	1	0,2
Hypotrophic lower extremities	1	0,2
Other findings	11	2,1

Source: Case database, field research team, National Institute of Health.

69.6% (360) of the cases were managed under emergency observation, receiving symptomatic medical treatment with remission of their clinical symptoms without documenting neurological deficits or signs of permanent focalization. 44.1% (228) of the cases returned to the emergency room between one and six times for the same symptoms (see table 15).

Table 15. Reconsultations to the ESE Hospital Nuestra Señora del Carmen, El Carmen de Bolívar, Bolívar, 2014.

Number of re-consultations	Frequency	Percentage (%)
0	289	55,9
1	114	22
2	54	10,4
3	35	6,8
4	13	2,5
5	10	2
6	2	0,4
Total	517	100

Source: case database, field research team, National Institute of Health.

4.3.4.5 Paraclinical analysis: a decrease in hemoglobin and hematocrit levels was documented with respect to the physiological parameters for age as well as the presence of an increase in the number and morphology of platelets in two of them.
In metabolic function tests, hypoglycemia levels (<60 mg/dL) are reported in 0.6% of cases. No results of deterioration of kidney, liver, muscle or immunological function were reported in the cases in which specialized tests were performed, nor the presence of antibodies against infectious agents.

Conventional diagnostic images such as chest and long bone x-rays do not report alterations that reflect heavy metal accumulation.
Specialized diagnostic images such as magnetic resonance imaging at the level of the central nervous system do not report structural alterations.
On the other hand, electrophysiology studies at the level of the peripheral nervous system and at the level of the neuromuscular plate do not report alterations in the cases reviewed.

4.4. Obtaining biological samples for the analysis of metal levels in girls with symptoms and their relatives.

The National Institute of Health, with the support of the clinical laboratory service of the ESE Hospital Nuestra Señora del Carmen, initially obtained 251 biological samples from patients with symptoms compatible with the event under investigation. Samples were also obtained from relatives of the patients who agreed to the procedure. Additionally, in the city of Bogotá, 20 samples were taken from the cases referred from El Carmen de Bolívar for specialized care in the clinical toxicology service of the San José Infantil Hospital and from one of their companions.

In the 271 case samples from the municipality of El Carmen de Bolívar processed in the environmental health laboratory of the INS Public Health Networks Directorate, no quantifiable levels of lead were detected in 27 of the processed samples. In the remaining 244, no values higher than the risk level of this metal in blood were found (<5 µg/dL in children and <10 µg/dL in adults).

It is important to highlight that two of the cases with a history of environmental exposure to automotive mechanics workshops did not present higher risk levels for blood lead concentrations.

On the other hand, the results of the analysis of aluminum levels in serum by atomic absorption reported by an external laboratory for 16 samples of girls from El Carmen de Bolívar were consolidated, which are within the range of serum levels expected for pediatric population.

4.5. Active institutional search (BAI)

80 codes were identified in the international classification of diseases tenth version (ICD-10) compatible with these clinical manifestations and with diagnoses such as anxiety disorders, neurological pathologies, signs and symptoms not classified elsewhere, intoxications, self-inflicted poisoning and Esavi. A retrospective institutional active search was carried out in the UPGD of the municipality for patients who consulted between January 1 and August 31, 2014.

4.5.1. Institutional active search results (BAI)

The municipality of El Carmen de Bolívar has six UPGD: ESE Giovanni Cristini of I level, ESE Nuestra Señora del Carmen Hospital of II level of care, IPS Saludcoop Carmen de Bolívar, IPS SaludVig, IPS comprehensive health, and IPS Celta. The two public institutions offer emergency services and outpatient consultation, while the private ones only offer outpatient consultation. In total, 938 medical records from four of the six institutions were reviewed.

According to the established criteria, it was found that 748 (79.7%) of the stories did not meet the case definition, 158 (16.8%) correspond to patients who were already identified as initial cases and 32 (3, 4%) correspond to subjects who meet the case definition (see table 16).

Table 16. Distribution of the classification of cases after the review of medical records with compatible diagnoses for UPGD, event of unknown etiology, El Carmen de Bolívar, Bolívar September 2014.

UPGD	Classification			
	Fails	Case	New case	Total
ESE Our Lady of Carmen	641	134	26 (70,2%) 3	801
Celta IPS	70	0	(8,1%) 1	73
IPS Saludcoop Corporation	17	16	(2,7%) 2	34
Saludvig	20	8	(5,4%)	30
Total	748	158	32	938

Source: Field Research Team, National Institute of Health

Of the 748 medical records reviewed, 17 people presented at least one of the 22 clinical manifestations, which corresponds to 2.3%. The most frequently reported symptom was respiratory difficulty (2.3%), followed by chest pain (2%), nervousness (1.7%), upper limb paresthesia (1.6%), headache (1.3%). and lipothymia (1.2%). Taking into account the period of evolution of the different clinical manifestations, the shortest time was five minutes (average 19.2 minutes), one hour (average 4 hours), followed by one day (average 5.3 days) and one month (average 1.8 months).

On average, patients consulted 14 days after the onset of symptoms, according to the data provided in the medical history. The first consultation found was on January 1, 2014 and consultations were more frequent in the month of March (23%), followed by May (19%).

4.6. Active search in schools (BA)

During the week of September 8 to 15, an active search was carried out in public and private schools in urban and rural areas based on the registry of the Integrated Registration System (Simat) provided

by the Municipal Secretary of Education. The fundamental objective of this search was to identify girls who had presented the symptoms that are part of the case definition of the unusual event of unknown etiology under study, with the fundamental characteristic that they had not consulted any of the municipality's IPS. 21 schools were visited, 14 located in the urban area and seven in the rural area; 16 public institutions and five private ones. Two case definitions were established to classify the students recruited within the active search in schools as a case compatible with the unusual event under study. A total of 583 surveys were applied, of which 453 met the case definition and 130 did not.

Source: active search in schools, El Carmen de Bolivar, 2014

4.6.1. Descriptive analysis of active search in schools

Of the total number of girls interviewed, 540 correspond to the urban area and 43 girls to the rural area. In the urban area, the ages of the girls recruited ranged between 10 and 19 years with an average age of 13 years, while in the rural area the ages of the respondents ranged between 11 and 16 years with an average age of 13 years. .

The distribution of cases according to the date of onset of symptoms in relation to the presence of the unusual event under study coincides with the peaks of the epidemic curve of case presentation identified by the health system, in the months of August and September 2014. ; However, the presence of two peaks of case presentation in the months of March and July 2014 is striking, which coincides with the dates of the HPV vaccination campaigns carried out this month in some of the schools in the municipality. In 66 records it was not possible to obtain the date of onset of symptoms (the girls did not remember it).

The school in which the highest number of girls who presented symptoms but who did not

who consulted the health service was the Gabriela Mistral Educational Institution (22.2%), followed by Giovanni Cristinni (18.7%) and the Holy Spirit (13.9%). Regarding the rural area, the highest proportion of cases is concentrated in the San Isidro Educational Institution (61.1%), this is the rural school whose headquarters are located closest to the urban center of the municipality. The school grades in which symptoms compatible with the unusual event occurred ranged from the second grade of primary school to the eleventh grade of vocational secondary school. In the rural area, cases of girls occurred between the fourth grade of primary school and the eleventh grade of vocational secondary school, both in the urban area and in the rural area, the highest proportion of vaccinated girls was concentrated in the ninth grade of high sch

A high proportion of students recruited in the search were found in schools that did not have a significant medical or pathological history. No statistical difference was found between cases from rural and urban areas with respect to the presence of relevant medical history (Chi square – X2- of 3.245).

Among the information reported by the students surveyed, difficulties were found in remembering the exact dates of immunization and very few carried the vaccination card among their documents. In the urban area, the highest proportion of vaccinated girls who presented symptoms received two doses (80.6%) of the HPV immunobiological, followed by those who received one dose (11.1%), three doses (8.1%) and There was one case in which the vaccine was not applied (0.2%). Similarly, in the rural area, the vaccinated girls who presented the most symptoms received two doses (61.1%), followed by those who received 3 doses (22.2%), four doses (8.3%), one dose (5.6%) and one case was found with five doses applied (2.8%).

For schools in the urban area, at least two doses of the vaccine had been administered in all educational institutions (403 girls with at least two accumulated doses of HPV vaccine). Among the girls recruited through active search in urban schools, one stated that she had not received any dose of the vaccination schedule. In the rural area

observed a similar behavior, the vast majority of girls received at least two doses of HPV vaccine (30 girls with at least two accumulated doses of HPV vaccine).

In the active search in schools, it was found that the symptom most frequently related to

The unusual event of unknown etiology was headache in both urban and rural institutions, followed by dizziness or vertigo in urban schools and paresthesias in lower limbs in rural schools; No statistical difference was found between urban and rural schools between signs and symptoms (see table 17).

Table 17. Symptoms and signs of the event of unknown etiology found in the active search of urban and rural schools, El Carmen de Bolívar, Bolívar, 2014

Symptoms of the unknown event	Classification		Rural (n=36)		RR	IC 95%
	Frequency	Percent	Frequency 99.78	Percentage		
Headache	462		32	88,89	1,122	1 - 1,26
Dizziness/Vertigo	263	56,80	20	55,56	1,022	0,75 - 1,38
Lower limb paresthesia	236	50,97	29	80,56	0,632	0,52 - 0,76
Upper limb paresthesia	120	25,92	11	30,56	0,848	0,5 - 1,42
Respiratory difficulty	92	19,87	12	33,33	0,596	0,36 - 0,97
Chest pain	83	17,93	15	41,67	0,43	0,27 - 0,66
Paralysis	12	2,59	2	5,56	0,466	0,1 - 2
Syncope 2.59	12		5	13,89	0,186	0,06 - 0,5

Source: active search in school, El Carmen de Bolívar, 2014

4.7 Review and analysis of the municipal record of HPV vaccination sessions carried out

The Carmen de Bolívar municipality has carried out the application of the phases in accordance with the implementation defined by the Ministry of Health and Social Protection. Taking into account the number of doses applied, when verifying their records it was identified that of the total number of first doses there is a record of 98.4%, of the second dose 94.7% and of the third dose the 100%, it should be noted that the municipality began the management of the HPV vaccine in a permanent program starting in 2014.

The history of vaccination against human papillomavirus in the group of girls and adolescents who presented the event of unknown etiology was verified with the vaccination card and with the records of the expanded immunization plan (EPI).
In accordance with the guidelines of the Ministry of Health and Social Protection, in the municipality of El Carmen de Bolívar since 2012 the vaccination against human papillomavirus (HPV) in phases; During the implementation of the three phases, adjustments were made to the scheme and target population for vaccination.

In total, during the three phases of vaccination, 9,139 doses of HPV vaccine were applied, of which 57.8% were administered as the first dose, 35.9% as the second dose and 6.4% as the third dose. . Of the total number of girls and adolescents (509) who met the case definition for the event of unknown etiology, a history of vaccination was documented with at least one dose applied in 52.2% of the cases, with two doses of vaccine on 44.84% of the cases and with the complete scheme 3.4% of the cases. According to the total doses of HPV vaccine that were applied between 2012 and 2014, 4.4% of the target population presented the event of unknown etiology (400/9139), being more frequent in girls and adolescents with a history of receiving the second dose of vaccine (10.3%). The average of

The age of girls who received at least one dose of vaccine is 14.1 years and the average age of those who have no recorded vaccination history is 14.7 years.

According to the location of the educational institution, there are no statistical differences between being in the urban and rural areas (RTA: 1.2 with 95% CI 0.94-1.46); with attack rates of 6.5% for the urban area and 5.6% in the rural area in girls and adolescents with or without a history of vaccination.

The most frequent clinical manifestations in patients who received at least one dose of vaccine They were headache in 82.8%, paresthesias in the lower limbs in 61%, paresthesias in the upper limbs in 47.3% and chest pain in 43%; However, patients without a vaccination record had headaches in 73.4%, lower limb paresthesias in 61.5%, upper limb paresthesias in 45%, and chest pain in 37.6%; There is a statistical difference with the presentation of nausea as a clinical manifestation in girls and adolescents with at least one dose of vaccine compared to those without registration (APR: 8.4, 95% CI 1.17-61.19) (see table 18).

Table 18. Differences between the clinical manifestations of girls and adolescents who presented the event of unknown etiology with and without a history of vaccination, El Carmen de Bolívar, Bolívar 2012-2014

Clinical manifestations	At least one dose of vaccine		No vaccination card		Rate ratio attack	IC 95%	
	And	No	And	No		THAT	LS
Paresthesias in lower limbs	244	156	67	42	0,9924	0.8389	1,174
Paresthesias in upper limbs	189	211	49	60	1,0511	0.8333	1,3257
Perioral paresthesias	35	365	14	95	0,6813	0,3805	1,2168
Headache	331	69	80	29	1,1275	0,9984	1,2732
Respiratory difficulty	74	326	30	79	0,6722	0,4654	0,9708
Nausea	31	369	1	108	8,4475	1,1663	61,1873
Vomit	19	381	2	107	2,5888	0,6118	10,9436
Chest pain	172	228	41	68	1,1432	0,8755	1,4927
Fever	10	390	2	107	1,3239	0,2946	5,9487
Dizziness/vertigo	116	284	29	80	1,09	0,7701	1,5429
fasciculations	9	391	2	107	1,2263	0,2689	5,5927
Hyperthermia	1	399	1	108	0,2707	0,0172	4,3217
Syncope	101	299	24	85	1,1468	0,7753	1,6963
Dysesthesia	15	385	1	108	4,0875	0,5459	30,6032
Joint pain	22	378	9	100	0,6661	0,3159	1,4046
Muscular weakness	66	334	12	97	1,4988	0,8413	2,6701
Lipotimia	53	347	20	89	0,7221	0,4519	1,1539
Those	2	398	1	108	0,545	0,0499	5,9546

Source: National Institute of Health, field research team

Finally, the patients who presented the event of unknown etiology on average started signs and symptoms 15.4 months after the third dose, with a minimum of 2.4 months and a maximum of 27.6 months; After reviewing signs and symptoms and due to the time elapsed between the application of the second dose and the presentation of the event (greater than two months), Esavi is ruled out as a reason for the girls' medical attention.

4.8. Environmental recognition visit of the municipality and main risk factors found by neighborhood and in educational institutions

A tour is carried out on Saturday, August 30, accompanied by the Municipal Health Secretary and an environmental sanitation technician from the Departmental Health Secretariat of Bolívar, to plan the field work and look for possible environmental risk factors for the community. A total of nine neighborhoods selected by the location of schools in their area, access areas to the municipality and presence of water sources are visited. Relevant findings include the absence of storage of chemical substances in the facilities of the schools visited; inadequate disposal of solid waste in most schools; deficiencies in the supply of drinking water to schools which requires the use of rainwater reserves, among other means; unpaved public roads; open-air bodies of water with weeds and that are not channeled to the municipality's sewage system; open-air garbage dumps and other solid waste (currently the area is sealed by the environmental authority of the area, Corporación Autónoma Regional del Canal del Dique –Cardique-).

4.8.1. Sanitary and environmental conditions in the educational institutions of El Carmen de Bolívar, 2014

During the visit to the different educational institutions in the municipality of El Carmen de Bolívar, a checklist was applied to the sanitary conditions of the schools. Of the 19 educational institutions where the checklist was applied, 84.2% have at least one school feeding program for students, where in its highest percentage (31%) the Colombian Institute of Family Welfare (ICBF) and the Municipal Mayor's Office contribute with school breakfasts and snacks for children enrolled in primary school and in some grades of baccalaureate. 26% of the educational institutions visited have adequate classroom infrastructure.

With respect to water supply, private institutions have aqueduct service, while in public institutions such as those in rural areas, the use of rainwater storage tanks predominates, which is used for both cleaning and human consumption. , without applying any purification treatment. In 63% of school institutions, garbage collection and disposal is carried out either by open burning or by the municipal cleaning service. In the inspection of the food preparation and conservation areas in educational institutions, 21% are in acceptable infrastructure conditions and have sufficient implements used for food preparation (counters, utensils, pots, plates and others). which are permanently being cleaned and disinfected.

5. DISCUSSION

The event of interest in public health of unknown etiology that occurred in the municipality of El Carmen de Bolívar was characterized by a clinical picture of tachycardia, headache, respiratory difficulty, hyperventilation, paresthesias in upper and lower limbs, syncope, fainting and dizziness, presenting as predominantly in girls and female adolescents, in the age group between 13 and 15 years. However, it is relevant to mention that eight male individuals met the criteria of the case definition of the event and six of the cases in the female population were ages outside the age groups targeted by the vaccination program against the virus.

human papillomavirus implemented in our country. Most of the clinical symptoms of the event resolved quickly without leaving sequelae, even when some cases recurred.

The various clinical analyzes performed on the affected patients showed the absence of physical alterations in the examination or significant alterations in laboratory tests, electrophysiological studies and diagnostic images. No disease is documented in people exposed to the same condition, finding a general state of physical, psychological or social tension or stress, where the stressful stimulus attributed or identified by the community has been the application of the HPV vaccine and in which The attention of multiple actors has contributed to the reinforcement and maintenance of this problem.
It is possible that the rapid spread of cases can be attributed to the transmission of the disease through audiovisual observational learning.

Within the relevant medical history in the individuals related to the event, cases with previous pathological conditions similar to the clinical picture under study in months prior (3 to 16 months) to the administration of the HPV vaccine stand out.
On the other hand, the presence of psychiatric pathologies is highlighted in some cases of the event under study, such as suicide attempts, probable sexual abuse and depression.

With respect to its geographical distribution, the cases come mainly from the urban area, and belong to the subsidized social security regime, findings that are consistent, the largest urban distribution of the population is insured under the subsidized regime due to the labor informality that exists in the municipality (2). The spatial distribution of cases by neighborhood of residence shows that they are concentrated in the northwestern area of the municipality, but when analyzing their appearance by date of onset of symptoms, a specific pattern of geographical dispersion of the same is not found. In particular, cases in rural areas present the onset of symptoms with a low frequency in the month of July and a subsequent increase in the month of August in the urban area.

In the event of unknown etiology, approximately three individuals fell ill for every hundred enrolled in the educational institutions of El Carmen de Bolívar from the beginning of the year until mid-October, according to the date of onset of symptoms with the appearance of the index case during epidemiological week twenty-two and a progressive increase in cases that trigger the alert, with four main episodes standing out that allow an increase in cases to be recorded. In each episode, external events occur that in some way can influence the progressive increase in the occurrence of cases and increase the risk of other people presenting the event, such as the visit of representatives of national authorities to the municipality, the arrival of the specialized clinical toxicology group, media coverage, interspersed with periods of decreased frequency such as weekends, patron saint holidays and school breaks.

During the beginning of the alert (first episode) the cases mostly come from the same educational institution and initially a food-borne illness is suspected, however the appearance of cases is continuous although they decrease in the following week to less than the half of the initial report and in this period of time the possibility of reviewing possible lead poisoning or an event supposedly attributed to vaccination is contemplated. Subsequently, an average of one case per week occurs until the beginning of epidemiological week thirty when the second episode begins with the occurrence of sixteen new cases; It should be noted that this period coincides with the activities to support the alert at the national level and the assessment of individuals by specialists; In the week following this event, a notable decrease in cases was recorded and maintained.

The third episode covers epidemiological weeks thirty-three to thirty-five, with the appearance of 261 new cases, weeks in which different activities were carried out such as referral to a higher level of health care and visits to the higher level.

national Ministry of Health and Social Protection and National Institute of Health mainly from decision makers, which decreases in the last days of this period. The next episode occurs between epidemiological weeks thirty-six and forty with the appearance of 143 new cases; period that coincides with different events that occurred such as intervention by the National Institute of Health, visits by directors of the Ministry of Health and Social Protection and the governor of the department of Bolívar, in addition to the evaluation of patients by specialists. During this period, September 12 and 13 stand out with the occurrence of 27 cases, dates that coincide with the visit to the municipality made by a senator of the Republic. Finally, cases decreased significantly during week forty-one corresponding to the week of recess in educational institutions.

The behavior of the event according to the date of onset of symptoms allows us to characterize an epidemic curve of propagated source given by periods with a progressive increase in the appearance of cases interspersed with periods of low presentation of the same, which contrasts with what is expected for an exposure of the study population to a common point source of exposure, such as water consumption, food intake, exposure to chemical substances or the application of a medication or vaccine, generating an explosive epidemic shortly after being in contact with the etiological agent of the event. Epidemic outbreaks from a spread source are also characterized by the transmission of the event from person to person, which means that they may have a spread over time compared to those of common origin, a characteristic that occurs in the outbreak that occurred in the municipality of El Carmen. of Bolívar (3).

In this type of event, it is important to recognize that the wide dissemination that the national and international media have given to this health event under study has eventually magnified its effect on the population, especially when one of the hypotheses that it handles community affected is about the use of the HPV vaccine in girls and adolescents. This situation has already been described on other occasions as the “Weber Effect”, which mentions that the increase in the reporting of adverse events to a medical treatment, in this case, the use of a vaccine, corresponds to factors such as its release to the market, the type of population to which it is directed (in this case the mechanism of HPV transmission, of a sexual nature and the population targeted by the vaccination campaign) and the presence of some type of health alert about it that has been issued. (4).

It cannot be ignored that after the authorization of use of the vaccine by the FDA, the media coverage that has been given to its possible mild and serious adverse effects where its use has been authorized is quite extensive, information that is available. willingness to be reviewed by the general community through media such as the Internet, television and written press. There are even studies that have shown a correlation between the publication of news in relation to potential adverse events of the vaccine and the presentation of Esavi in the community that is the focus of that news (4). Another situation that deserves special attention is the availability, especially on the Internet, of information without the support of any academic or research body; Some web pages present information that has not been sufficiently reviewed and validated and that may eventually lead some readers to misinterpret that information and assume possible adverse effects (in our case, the administration of the HPV vaccine) due to its use. of some health technology. The greatest danger of this situation is the “word to voice” process that can perpetuate the process of disturbing the source of information, confusion and thus increase the fears and anxiety of the individual or a community (5).

Similar situations have occurred in an outbreak of epidemic hysteria among high school students in San Juancito, Francisco Morazán, Honduras where there was extensive media coverage that classified the problem as pesticide poisoning. However, in view of

that an identifiable cause was not evident as the investigation progressed and the recent history of the outbreak in the neighboring municipality, the different communications pointed to the impossibility of determining the causal agent, thus generating greater anxiety among parents and the community. This is a fact that has also been reported by other authors (6, 7) so social communicators must be instructed about the nature of these events so that public opinion can be adequately oriented (8).

At the beginning, different hypotheses were proposed that were discarded as the study of the outbreak progressed. When carrying out an analysis of the hypothesis of lead poisoning, raised by the presentation of predominantly neurological symptoms in the cases, it is important to highlight that alterations in other organic systems vulnerable to exposure were not documented in the clinical records or in the paraclinical studies. to this metal such as hematopoietic, renal and digestive, nor were diagnoses of metal poisoning in the population served identified through the search of care records in the institutions providing health services in the municipality.

On the other hand, with respect to the blood levels of lead obtained in the cases and adults in their family nucleus by the laboratory of the National Institute of Health, no concentrations of this metal in blood higher than the reference levels of possible risk were detected. for health (5 µg/
dL or more in children and 10 µg/dL or more in adults, CDC, 2012), nor were lead levels detected in the analytical results carried out by the National Institute for Food and Drug Surveillance (Invima) on the vaccine batches against HPV used in vaccination campaigns. On the other hand, the presence of a common source of lead exposure (large-scale industrial activities) in the urban or rural area of the municipality that could generate a risk to the entire population was not documented.

The findings described above allow us to rule out the possibility of widespread lead poisoning in the affected population. However, there are particular cases (two sisters) who

Prior to the analyzes carried out by the National Institute of Health, lead levels higher than the reference levels were reported in the analyzes carried out by private laboratories and to whom, during the visit to their homes, the existence of a junkyard in their homes was documented and they received chelation treatment by the clinical toxicology group of the San José Infantil Hospital of Bogotá. In these particular cases, it is important to carry out periodic clinical and laboratory monitoring to evaluate any medium-term health impact due to said environmental exposure.

Studies carried out on children residing in areas with high exposure to sources of lead contamination in Yumbo (Valle del Cauca) and Cartagena (Bolívar), report average concentrations of lead in blood higher than those of the present study (4.7 µg/dL and 5.5 µg/ dL vs. 1.5 µg/dL, respectively) using atomic absorption spectrophotometry with a graphite furnace and also finding blood and skeletal alterations in the children evaluated, findings that were not reported in the cases of the event in study (9,10).

On the other hand, exposure to the HPV vaccine adjuvant based on amorphous aluminum hydroxyphosphate sulfate at a concentration of 0.225 mg and the risks to human health have been evaluated by researchers such as Mitkus et al., who later From a review of the pharmacokinetics of aluminum in infants exposed through diet and vaccines, they conclude that exposure to aluminum through vaccines is lower than exposure through diet and some medications. In turn, there are other immunobiologicals from the expanded vaccination program of Colombia (PAI) and the world such as hepatitis B, Pneumococcus and Haemophilus influenza, whose aluminum content is higher (2.22 mg) and similar massive events have not been reported. which is under study (11).

The Global Vaccine Safety Advisory Committee of the World Health Organization in its March 2014 report analyzed the relationship between the HPV vaccine and autoimmune diseases.

based on a review of the evidence (12). As a result of this review focused especially on multiple sclerosis, aluminum as an adjuvant, vasculitis caused by DNA fragments from the vaccine and complex regional pain syndrome, it reaffirmed that the risk-benefit profile of the vaccine remains favorable. However, some alarming statements and anecdotal observations and reports without scientific rigor affect vaccination programs worldwide (13).

Regarding the hypothesis of suspected FBD, the investigation of the outbreak study revealed that there is no association between the foods consumed and the health status of the students at the Espíritu Santo school because not all of them consumed the same foods. Additionally, the results of the analyzes carried out by the Bolívar departmental public health laboratory were negative for pathogenic microorganisms. This allows us to affirm that there is no specific cause of any contaminated food or water with the symptoms reported by the students, similar to what happened in a study carried out in Honduras on high school students where the cause of the outbreak of collective hysteria was initially related to toxic substances. , food, water or an infectious process (14).

Likewise, the hypothesis raised about possible poisoning by pesticides due to their presence or recent use in the educational institution where the outbreak originated as well as in its surroundings was ruled out, given that in the environmental inspection visit carried out by The Bolívar Health Secretariat found no stored pesticides, empty packaging or records of recent fumigations in the school facilities.

This shows that there is no association of the event with the toxic effects of any pesticide, a situation that occurred in Atlanta where in an environmental study carried out in an elementary school no plausible toxic or infectious cause of the mass hysteria outbreak was found (15).

Given the non-specific clinical characteristics of the symptoms presented by the cases, it was proposed the hypothesis of intoxication due to the consumption of psychoactive substances. However, when performing the analyzes on five of the girls from the initial outbreak, no quantifiable levels were detected for five groups of substances, therefore the association of this factor with the etiology of the outbreak is ruled out.

Due to comments from the community in which some people stated that the girls associated with the outbreak "were possessed" by the use of the Ouija board, it was included as a hypothesis, but it was discarded because in the interviews carried out with the students, parents and teachers were not recorded playing prohibited games; ruling out an association with the event under study. These types of factors have been associated with massive outbreaks in other countries, such as what was reported in India, where they described a rare outbreak of a massive family psychogenic event in the context of strong religious and cultural beliefs that affected 10 members who presented somatoform disorders, recurrent vomiting. , conversion and possessive attacks (16).

Regarding the HPV vaccine, it has been studied in thousands of people in many countries around the world which showed no serious safety concerns and indicated that it is safe. Common mildly negative reactions that were reported during these studies included pain at the injection site, fever, dizziness, and nausea.

A meta-analysis that included 46 publications (including 13 randomized clinical trials), evaluated the short- and long-term effects in the prevention of lesions associated with HPV infection and, among other aspects, evaluated the safety of the vaccine in the patient cohorts addressed (17). Fourteen studies addressed the issue of vaccine safety, its administration and the appearance of adverse events. It was found that there are no statistical differences in the appearance of serious side effects, comparing the group that was administered the vaccine against a group who was administered a placebo (pooled RR of 0.99, with 95% CI of 0.91-1.08).

Regarding the debates about the safety of the vaccine, the vast majority have been developed around the components of the vaccine, among which are the "adjuvant system 04" or SA04 (combination between the lipid 3-0-desacyl-4'- monophosphoryl and an aluminum salt) which is useful in increasing the immune response to the administration of the vaccine.
This characteristic is what has been widely discussed given that theoretically this compound could exacerbate some type of immune response in the recipient's body and facilitate the presence of some autoimmune clinical condition. In fact, a study carried out on 68,512 volunteers (18) compared two populations, one of which was administered the adjuvant system while the control group did not use the aluminum salt. Finally, no statistical differences were found regarding the appearance of autoimmune diseases, with respect to the use or not of aluminum salts in the adjuvant complexes (RR 0.98 with 95% CI of 0.80 - 1.21).

In the United States (one of the first countries to endorse the use of the vaccine in its population) various studies have confirmed that the administration of the quadrivalent HPV vaccine is safe for the health of the recipients, in addition to the benefits in prevention, among others, of cervical cancer.
Since 2006 and March 2014, nearly 67 million doses of this immunobiological have been administered, after which a total of 25,176 cases, 92.4%, have been reported to the Vaccine Adverse Event Reporting System (VAERS). of which have been classified as mild and expected events after inoculation, among which local pain at the puncture site, dizziness and headache stand out. None of these events are usually repetitive and have not left any consequences. It should be noted that the VAERS is a passive surveillance system and is aimed at the use of the general population, in which both clinicians, patients and family members can make reports of possible side effects to vaccines, which is why it cannot be conclude for each case that the health situation presented is actually due to the administration of the vaccine under consideration (19). According to the information found in

In our study, 9,139 doses of vaccine were administered in the municipality and 4.4% of girls and adolescents presented two or more clinical manifestations; However, difficulties were found in the registration of vaccination, a situation that may reduce the magnitude of the denominator.

The most frequently reported clinical manifestations as effects of HPV vaccination were erythema at the application site, nausea, dizziness, and fainting (20). In the case of girls and adolescents from El Carmen de Bolívar, nausea showed a greater frequency in girls with a history of having received at least one dose of vaccine, compared to the population without this history, the rest of the clinical manifestations were distributed in the same way in the two groups.

In Spain, a telephone follow-up was carried out on 2,124 women vaccinated against HPV, of which 22% manifested some symptoms after vaccination, with fever, inflammation, local pain and redness being more common and of these more than 46% occurred with the first dose. In our study, the most frequent clinical manifestations were paresthesias in extremities and headache, which were mostly related to the second dose of vaccine, contrary to reports found in other studies (21).

In 1998 in Jordan, the occurrence of symptoms such as headache, nausea, dizziness, hyperventilation and fainting was reported; The teachers reported the event, achieving the transfer of the students in ambulances and the investigation of the possible origin of the event. As a background, 160 tenth grade students received the Td tetanus and diphtheria vaccine. The news spread quickly in the neighborhood and on the second day of the start of the outbreak, 806 minors were found with symptoms (22). This situation is similar to what happened at the beginning of the event in the department of Bolívar, where the majority of the girls affected came from the same educational institution, were on average 14 years old, were most affected by vocational secondary courses and not all with a history of HPV vaccination.

More recently in 2002 in China, 900 students between 7 and 16 years old were hospitalized due to symptoms such as fever, nausea and vomiting. The students did not present abnormalities in the physical examination or alterations in laboratory tests; The precedent that became most relevant was the vaccination against Japanese encephalitis of 8,300 minors (23). Of the 517 cases of El Carmen de Bolívar, no important findings were found in the clinical or laboratory examinations, the recovery of symptoms was rapid and even without the administration of medications, and relapses were more frequent on dates of greater presence in the municipality of media and departmental and national entities.

On the other hand, it is worth highlighting the importance of the active search exercise for cases that were not consulted or that were not identified by the health services of the municipality, where it was possible to characterize 453 girls who stated that they had presented at least one clinical episode that fit the case definition of the present study. Attention was drawn to the absence of significant medical history among the identified girls, the greater concentration of cases and impact of the events in schools in the urban area and of a public nature in the municipality, and the presentation of cases of the unusual event under study on dates similar to those that were described in the epidemic curve of cases captured through health services.

Given these findings and the diversity of social, environmental and cultural factors that are part of the environment in which the population of children and adolescents in the municipality develops, there is no evidence to affirm that said common source of exposure explains the presence of the condition. clinical presentation is due, in particular, to the administration of the HPV vaccine. The above can be explained based on the multiple clinical studies that have supported not only the safety of the vaccine in the population targeted for vaccination, but also the presence in a minimum proportion of side effects which, in general, are of intense intensity. mild, self-limited and not they leave consequences. Vaccine safety studies have led to the vaccination schedule being included in 28 national vaccination plans in the world (24).

On the other hand, some meta-analyses have shown that the safe administration of this immunobiological provides protection against the appearance of neoplastic lesions secondary to infection by the HPV serotypes for which the vaccine has been synthesized. Likewise, the presentation of mild adverse events is usually very low and, if present, is related to the clinical manifestations expected after the administration of any immunobiological; In that sense, if the conditions of administration of the vaccination schedule are regulated under a national guideline, the unusual and focused presence of cases in a period of time and in a similar geographical space would not be expected (25).

In Colombia, any geographic area whose population is affected by health situations with cases of unusual frequency requires an epidemiological study of the situation based on protocols established in the National Public Health Surveillance System and the application of quantitative or qualitative methodologies; That is why a large outbreak study was developed that would allow a complete initial approach to all the possible etiological factors of the event, particularly due to the impact of a susceptible population group such as children and adolescents in a community.

A relevant aspect of the demographic and social profile of the municipality is that young people represent 25% of the general population and 31% of the active productive population that is concentrated in the municipal seat, mostly belonging to socioeconomic level I of the health system. identification of potential beneficiaries of social programs such as families and youth in action; state programs that prioritize health care and education for victims of violence. However, there are no strategies in the municipality that allow these individuals to be linked to work life or higher education upon completion of secondary studies, a situation reflected

in the low percentage (4.1%) of graduated students who immediately enter higher education in other cities (2).

Since it was not possible to test any of the proposed hypotheses, it is necessary to rethink the study, identify new variables by restating the study hypotheses. According to the findings found in the outbreak study, it is considered necessary to carry out a case-control study in order to determine other factors or possible exposures that are generating this public health problem.

4. The student population enrolled in the municipality of El Carmen de Bolívar is made up of 48.03% women, the highest percentage of which (37.8%) is concentrated in the age groups of 10 to 14 years. and belongs to socioeconomic stratum one.

5. 517 patients who met the case criteria were identified, presenting predominantly in girls and female adolescents and in the age group between 13 and 15 years during the study period. However, it is relevant to mention that cases occurred in males and in women with ages outside the age groups targeted by the human papillomavirus vaccination program implemented in our country.

6. CONCLUSIONS

1. An outbreak study was carried out in the municipality of El Carmen de Bolívar, notified to the National Institute of Health during epidemiological week 22 (May 30), through the application of different activities to achieve its characterization and determine the possible factors. of risk associated with the unusual event of unknown etiology.

2. The presence in the municipality of El Carmen de Bolívar of social and economic situations that can affect the population dynamics is documented, among which the following stand out: victims of violence, displacement, large percentage of SISBEN families, low family income, informality labor and child labor.

3. There are environmental risk factors that can generate a negative effect on the health of the population of the municipality of El Carmen de Bolívar such as: lack of drinking water coverage in some sectors, lack of an adequate sewage drainage system, presence of bodies of stagnant water that favor the presence of vector breeding grounds, deficiencies in the collection of garbage and solid waste, establishment of illegal garbage dumps, lack of a market place and an animal benefit plant that meets adequate sanitation and presence of flood risk areas.

6. The spatial distribution of cases by neighborhood of residence shows that these are concentrated in the northwestern area of the municipality, where the educational institutions with the highest number of cases are also located (Espíritu Santo, Gabriel García Taboada, Giovanni Cristini). However, when analyzing the appearance of these by date of onset of symptoms, a specific pattern of geographical dispersion of the same is not demonstrated.

7. The epidemic curve prepared by analyzing the date of onset of symptoms highlights different periods of a higher frequency of cases, being typified as a propagated source curve given the progressive increase in the appearance of cases in waves. In the review of cases prior to the initial group of cases, a low frequency of presentation was found since the months of January and February 2014.

8. A medical history of previous similar clinical conditions, neurological and mental health diseases was documented, which in some cases occurred before the administration of the HPV vaccine.

9. The event of public health interest of unknown etiology that occurred in the municipality of El Carmen de Bolívar was characterized by a clinical picture of

acute presentation of headache, respiratory distress, hyperventilation, paresthesias in upper and lower limbs, syncope, fainting and dizziness, with an evolution without sequelae and in most cases without finding any alterations in the physical examination or in the paraclinical tests performed, but with a significant percentage of re-consultations for the same condition.

10. None of the biological samples taken for the quantification of blood lead levels in girls and adult companions from the municipality of El Carmen de Bolívar, levels were found that exceeded the values recommended by the Center for Disease Control and Prevention (CDC) of the United States to cause a risk to human health (5 µg/dL or more in children and 10 µg/dL or more in adults), therefore the hypothesis of possible poisoning by heavy metals, specifically lead, is discarded.

7. RECOMMENDATIONS

1. Strengthen the early identification of cases reported by the community by expanding the active institutional search in health service institutions other than the ESE Hospital Nuestra Señora del Carmen.

2. Support in the generation of an inter-institutional strategy to address a comprehensive community intervention, given the social and economic situations that may affect the dynamics of the population.

3. Carrying out an analytical study of cases and controls that allows addressing exposures prior to the presentation of the event.

4. Support in the generation of a risk communication strategy for the community as well as for the media, with the aim of reducing the impact of misinformation on the health situation of the community.

5. Follow up on cases that present risk factors for environmental lead poisoning with blood levels greater than 5 µg/dL (pike habit, presence of sources or industrial activities within or near residential areas, child labor, deficits nutritional and others), recommending reevaluation in one year.

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