

Epidemiological Characteristics in Patients with Diphtheria in the Autonomous Service University Hospital of Maracaibo

Elizabeth Castro

Faculty of Medicine, University of Zulia, Maracaibo, Venezuela

Email address:

eliza_castro_04@hotmail.com

To cite this article:

Elizabeth Castro. Epidemiological Characteristics in Patients with Diphtheria in the Autonomous Service University Hospital of Maracaibo. *Science Journal of Clinical Medicine*. Vol. 10, No. 4, 2021, pp. 113-119. doi: 10.11648/j.sjcm.20211004.16

Received: August 29, 2021; **Accepted:** November 9, 2021; **Published:** November 17, 2021

Abstract: Diphtheria is a notifiable infectious disease caused by *Corynebacterium diphtheriae*. Objective: To establish the epidemiological characteristics in patients with diphtheria in the Autonomous Service University Hospital of Maracaibo. Methodology: Descriptive, cross-sectional, prospective and field research. The sample was represented by patients older than 15 years admitted to the Internal Medicine service. Results: Between January 2018 and December 2018, 67 patients were included, the incidence was 25 cases per million inhabitants, 58,2% were female, aged between 15 - 65 years. 92,5% did not travel in the last month, 19,4% reported having had contact with diphtheria. Most of the cases came from the Maracaibo municipality in 46,3%. The predominant educational status was complete secondary with 59,7%. 86,6% do not know their vaccination history. The current occupation that prevailed was merchant in 34,3%, followed by housewife 23,9% and student 17,9%. The socioeconomic status by the Method of Graffar Méndez Castellano, the working class stratum IV predominated with 77,6%. The time elapsed from the onset of symptoms to hospitalization was 1-15 days. Tonsillitis-like respiratory form as a typical clinical presentation in all cases; fever, dysphagia, and presence of adherent pseudomembrane predominated in most patients. 22,4% presented complications. Most of the cases were confirmed clinically 77,6% while 4,5% were laboratory confirmed. The fatality rate was 19,4%. Conclusion: Diphtheria is a re-emerging disease in Venezuela in recent years, it affects any age and sex, in addition, it has been associated with low vaccination coverage and low socioeconomic status, so prevention and control is essential to eradicate the disease.

Keywords: Epidemiological Characteristics, Patients with Diphtheria, Diphtheria

1. Introduction

Diphtheria is a notifiable, infectious disease caused by aerobic, non-encapsulated, non-spore-forming, nonmotile, pleomorphic Gram-positive rods, *Corynebacterium diphtheriae* (*C. diphtheriae*). It mainly affects the upper respiratory tract, another form of presentation is cutaneous diphtheria, and this is less frequent. If not caught early and treated promptly, it can lead to significant mortality from its complications [1].

In India, in 2016, a case-control study of diphtheria in the city of Hyderabad, reported 63 cases and 63 controls, the age range was 10-45 years, with a median of 21 years, there were no statistical differences in regarding gender, in terms of occupation, 49% were students, 15% did not have a job.

Approximately 15% to 20% of cases and controls have never attended school. Between cases and controls there were no significant differences in sociodemographic and economic characteristics [2]. In 2017, in North Karnataka, India, 432 cases were reported, of which 38 (8,79%) had a positive culture for *C. diphtheriae*, of these 55,26% belonged to the 1-5-year-old group and 36,84% were between 6 and 10 years old. Of the confirmed cases, men were three times more than women, patient mortality data were not available [1]. In South Africa, in 2017, a total of 15 cases were reported, of which 11 were confirmed diphtheria, there was no travel history between the cases, the age range was 4 to 41 years, with a median age of 10 years. 60% were male. 93% presented tonsillitis / pharyngitis as a clinical sign, followed by fever in 73%. In 67% of the cases a pseudomembrane was

visualized. 75% had been incompletely or never immunized. 2 cases had no vaccination records and were classified as unknown. The reported case fatality rate was 27% [3].

In England, in 2014, there were 20 cases of diphtheria, 55% were adults over 45 years of age; 55% were women. 60% of the toxigenic isolates were identified as *C. ulcerans*, where contact with animals was the predominant risk factor; the remaining 40% were caused by strains of *C. diphtheriae*. 7 cases had a recent travel / immigration history; 6 had stayed in a country where diphtheria was endemic. None of the *C. diphtheriae* cases were fully immunized. 5 cases resulted with cutaneous diphtheria and the rest respiratory cases, of these 3 had a sore throat, one of which had "classic" diphtheria with pseudomembrane. The fatality rate was 10% [4]. In Mayotte, a French department, it is an island of the Comoros archipelago, with a low socioeconomic level, 14 cases of diphtheria were reported in 2017, the age range was 2 months-39 years, the average was 11 years, of which 11 cases were men, 8 patients had recently emigrated (most within 1 month) from neighboring islands. 13 cases presented cutaneous diphtheria and one case presented respiratory symptoms [5].

In the Dominican Republic, in 2015, 145 cases of diphtheria were reported, of which 80 (66%) met the definition of the case, the age range varied from 3 months to 13 years, with a mean of 3 years, the 62,5% were male. Cutaneous diphtheria was not reported in this outbreak. The average annual incidence of diphtheria was 4,91 cases per million people from 2000 to 2003, rose to 8,8 cases per million during the years 2004 and 2005, and decreased to 0,38 from 2006 to 2014; no cases of diphtheria have been reported since 2011. Vaccination coverage ranged from 72 to 81% from 2000 to 2004 and from 81 to 89% from 2005 to 2013. The case fatality rate was 32,5% [6]. In Haiti, the outbreak that began in late 2014, until February 2018 reported a total of 410 probable cases of diphtheria. The fatality rates were 22,3% in 2015, 27% in 2016 and 10,7% in 2017 and 2018. Women represented 57% of all cases in 2015; in 2016 no differences were observed by gender, for 2017 women represented 60% and 47% in 2018 respectively. 64% of the probable cases reported between 2017 and 2018 are under 10 years of age [7].

In Brazil, in 2014, 174 cases of diphtheria were reported, of which 27 cases were confirmed, 9 cases were confirmed by laboratory, 7 by clinical criteria and 11 by clinical-epidemiological criteria, most of the confirmed cases occurred in children and adolescents under 15 years of age, with 18 cases predominantly female. 16 cases had been partially immunized and 10 fully immunized. In 25 cases, the predominant clinical sign was the formation of a pseudomembrane in the tonsils. 4 cases reported lower limb paralysis as a complication. 3 cases ended in death [8].

In Venezuela, since 1992 no cases of diphtheria were reported until 2016 according to the epidemiological bulletin issued by the Ministry of Popular Power for Health (MPPH), for epidemiological week number 52; 3 cases of diphtheria were reported in Venezuela, with a cumulative of 324 cases

[9]. However, until epidemiological week number 5 of 2018, a total of 969 probable cases were reported (324 cases in 2016, 609 in 2017, and 36 in 2018), of which 726 were laboratory confirmed and 113 died (17 in 2016 and 96 in 2017); with a mortality rate of 15,5% [7]. Few data are known about the epidemiological aspects of this reemergence, so this study has the general objective of establishing the epidemiological characteristics in patients with diphtheria in the Autonomous Service University Hospital of Maracaibo, and specific objectives to determine the incidence of diphtheria, classify patients according to sociodemographic and economic characteristics, describe the clinical and laboratory characteristics, calculate the fatality rate in patients admitted with a diagnosis of diphtheria.

2. Literature Review

The causative agent of the disease was first described in 1883 by Klebs and in 1884 Loeffler succeeded in cultivating the bacteria [10]. The bacteria have a characteristic mallet-shaped bacillary appearance and usually form clusters of parallel lines, or palisades, known as "Chinese characters." There are four biotypes of *C. diphtheriae* capable of causing diphtheria (mitis, intermedius, belfanti, and gravis), based on colony morphology, hemolysis, and fermentation reactions [11]. In 1888, Roux and Yersin discovered the toxin produced by *C. diphtheriae* [10].

Throughout history, diphtheria has been one of the most feared infectious diseases in the world, causing devastating epidemics, mainly affecting children. In the 1880s, in Europe and the United States of America (USA) the fatality rates reached 50% in some areas, with the use of diphtheria antitoxin (DAT) treatment the fatality rate in Europe decreased about 15%. Diphtheria toxoid-based vaccines became available in the late 1940s in Europe and the USA in the 1970s, before these vaccines were easily accessible and used worldwide, an estimated 1 million occurred diphtheria cases and 50,000-60,000 deaths each year in low- and middle-income countries. After the establishment of the Expanded Program on Immunization (EPI) in 1974, with the diphtheria vaccine as one of the original 6 EPI vaccines, the incidence of diphtheria decreased dramatically around the world. The total number of reported diphtheria cases decreased by > 90% during the period 1980-2000 [12].

After the introduction of a primary series of childhood diphtheria vaccination in a population where diphtheria is endemic, 2 epidemiological stages have been described. In the first stage, the incidence of the disease changes from a predominantly preschool pattern to a higher proportion of cases in school-age children. In the second stage, cases are seen mainly in adolescents and young adults > 15 years [13]. Infection in infants younger than 6 months is rare due to the presence of maternal antibodies. Diphtheria remains a significant health problem in countries with poor routine vaccination coverage. In regions with temperate climates, most cases occur during the cold season, while in warmer climates transmission occurs throughout the year [12].

After an incubation period of 2 to 4 days, signs and symptoms of local inflammation develop [14]. It mainly affects the upper respiratory tract, another form of presentation is cutaneous diphtheria, however, the most frequent form of presentation is tonsillar or pharyngeal diphtheria, sore throat is the early universal symptom: only half of the patients present fever, and a few have dysphagia, dysphonia, malaise, or headache [1]. The virulence of the organism resides in its ability to produce the potent polypeptide exotoxin, which inhibits protein synthesis and causes local tissue necrosis, which becomes a gray-brown, leather-like adherent pseudomembrane that is difficult to remove and then a bleeding and edematous submucosa. The underlying soft tissue edema and lymphadenopathy may present a bull neck appearance. The absorption of the toxin can lead to systemic manifestations: necrosis of the renal tubules, thrombocytopenia, cardiomyopathy and / or demyelination, these last two complications can occur between 2 and 10 weeks after mucocutaneous infection [14].

The clinical diagnosis of diphtheria is based on the presence of pseudomembranous pharyngitis. Laboratory tests consist of: (1) Culture on blood agar and media containing tellurite, Tinsdale media. (2) The diphtheria toxin (tox) gene can be detected directly in *C. diphtheriae* isolates using polymerase chain reaction (PCR) techniques. (3) The modified Elek immunoprecipitation test for toxin detection; this standard test takes 24 to 48 hours. A positive culture with toxin-producing *C. diphtheriae* confirms the etiologic diagnosis [12]. Although laboratory investigation of suspected cases is recommended for case confirmation,

treatment should be started immediately without waiting for laboratory results as diphtheria, if not detected early and treated promptly, can lead to significant mortality due to its complications [1].

3. Materials and Methods

A descriptive, prospective and cross-sectional research was carried out, with a field design. The population and sample was represented by all those patients older than 15 years admitted with a clinical diagnosis of suspected diphtheria cases in the Internal Medicine Service of the Autonomous Service University Hospital of Maracaibo, in the city of Maracaibo, Zulia state, in a period from January 1 to December 31, 2018. The following were excluded: (1) Patients under 15 years of age. (2) Patients who did not meet the definition of a suspected diphtheria case. See table 1 for definition of diphtheria case. (3) Patients who do not agree to sign the informed consent.

Data were collected through an epidemiological file and socioeconomic status was determined using the Graffar-Méndez Castellano method: upper class, upper-middle class, middle class, working class, extreme poverty [16]. The statistical analysis of the results was carried out using the Statistical Program for the Social Sciences, SPSS, version 15.0 for Windows, the data obtained are expressed with descriptive measures, percentages were calculated from the frequency of appearance in regard to the categorical variables. Measures of central tendency and standard deviation were used. The data were expressed in tables and figures.

Table 1. Definition of diphtheria case.

Case Classification	Definition
Clinical	Person with any of the following clinical forms: (1) Respiratory Diphtheria: Patient with an acute disease of the tonsils, pharynx and / or nose, characterized by one or more confluent and invasive adherent grayish plaques, with a surrounding inflammatory area of color dull red, sore throat, swelling of the neck, fever, headache and variable degree of compromise of the general condition. (2) Cutaneous Diphtheria: chronic non-progressive ulcerative lesion that may appear with a grayish membrane. (3) Diphtheria of other sites: lesion in the conjunctiva or mucosa [15].
Suspicious	Patient with a clinical picture of diphtheria, with the presence of plaques or membranes adhering to the mucosa [15].
Probable	Case that meets the criteria of the clinical definition and that has direct or indirect contact not confirmed by laboratory, but that comes from a risk area, in which it is also not possible to demonstrate a complete vaccination scheme (pentavalent or toxoid diphtheria-tetanus) [15].
Confirmed	Case that has been laboratory confirmed by isolating a toxigenic strain of <i>C. diphtheriae</i> , or with an epidemiological link with a laboratory confirmed case [15].

4. Results

The population consisted of 98 patients admitted with a clinical diagnosis of a suspected case of diphtheria, of which 18 were excluded because they were under 15 years of age and 13 patients were excluded due to clinical-laboratory discarding, leaving the sample made up of 67 patients admitted to the Autonomous Service University Hospital of Maracaibo with a diagnosis of a suspected case of diphtheria, between January 2018 and December 2018, the incidence was determined, obtaining 25 cases per million inhabitants in the State of Zulia, the distribution per month was: January 14,9%, February 10,4%, March 7,5%, April 1,5%, May

1,5%, June 6,0%, July 17,9%, August 14,9%, October 10,4%, November 9,0%, December 6,0%, appreciating two peaks in January and July respectively (Figure 1).

Regarding the sociodemographic characteristics (Table 2), 58,2% were female and 41,8% male, aged between 15 - 65 years, with a mean of 32,16 years. 7,5% had a recent travel history, travel days between 3-20 with a mean of 7,80 days; the place where they traveled: La Guaira (from Cabimas), Maicao (from San Francisco), Mene Grande (from Lagunillas) and Sinamaica (from Alta Guajira) and Villa del Rosario (from Jesus Enrique Losada). Only 19,4% reported having had contact with diphtheria. No relationship was found between those who traveled and those who reported contact with diphtheria. Most of the

cases came from the Maracaibo municipality in 46,3%, followed by Lagunillas 22,4%, Cabimas 6,0%, Mara, Jesus Enrique Losada and San Francisco with 4,5% each, then Cañada de Urdaneta, Guajira and Rosario de Perijá with 3,0% each, the rest coming from the Miranda and Valmore Rodríguez municipalities with 1,5% respectively. The level of education, only 1,5% turned out to be illiterate, the predominant level of education was complete secondary with 59,7%, followed by incomplete secondary with 16,4%, complete technical education 7,5% and incomplete 3,0% and university with a similar distribution, complete 6,0%, and incomplete 3,0%, 3,0% had complete primary as a degree of instruction. 86,6% do not know their vaccination history while 7,5% were incomplete, only 6,0% presented their complete vaccinations.

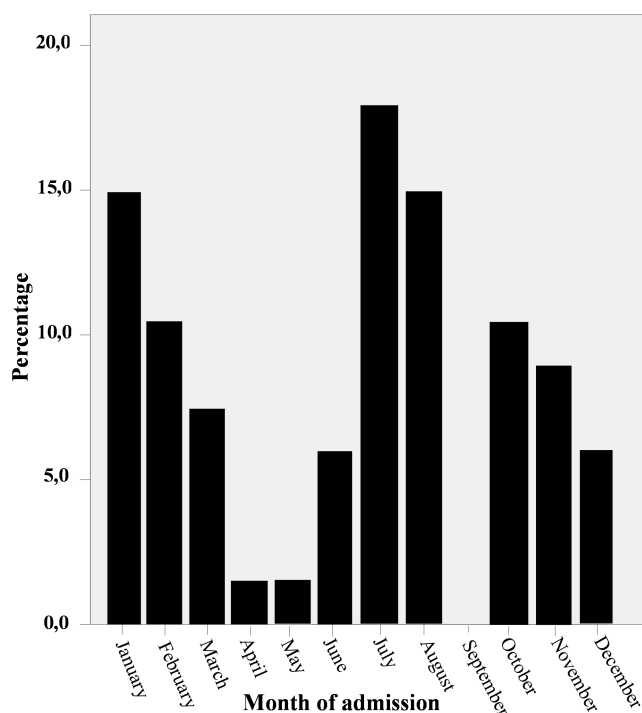


Figure 1. Distribution by month of the sample.

Regarding the economic characteristics (Table 3), the current occupation that prevailed was merchant in 34,3%, followed by housewife 23,9%, student 17,9%, the rest lawyer, bricklayer, pharmacy assistant, bionalist, shrimp, crab, accountant, shipper in oil, homeless, nurse, military, policeman, fisherman, secretary, school transporter, no occupation, with a similar distribution of 1,5% each. The socioeconomic status by the method of Graffar Méndez Castellano, the working class stratum IV predominated with 77,6%, followed by stratum V extreme poverty with 13,4% and middle class stratum III 9,0%; none of them in the upper class or upper-middle class, strata I and II respectively.

Regarding the clinical characteristics of the patients at the time of admission, taking into account the time elapsed from the onset of symptoms to hospitalization, it was 1-15 days, with a mean of 3,58. Tonsillitis-like respiratory form being the typical clinical presentation in all cases; clinical

manifestations such as: fever occurred in 89,6%, dysphagia 100%, dyspnea 31,3%, presence of adherent pseudomembrane in 100%, stridor 6,0%, bull neck 41,8%. 37,3% received diphtheria antitoxin. 22,4% presented complications, such as: acute respiratory failure in 14,9%, acute kidney injury 4,5%, toxic cardiomyopathy in 4,5% and toxic neuropathy 4,5%. Taking into account that the hospital stay varied from 0-29 days, with a mean of 11,18 days. Most of the cases presented clinical diagnosis 77,6%, while clinical - epidemiological was 17,9% and laboratory 4,5%. 67,2% were discharged due to medical discharge, while 19,4% died, 13,4% withdrew against medical opinion. The fatality rate was 19,4% (Table 4).

Table 2. Sociodemographic characteristics of the patients.

Incidence	25 cases per million inhabitants.	
Age (Mean)	15-65 (32,16)	
Sex	Frequency	Percentage (%)
Female	39	58,2
Recent trips in the last month	5	7,5
Days I Travel	3-20 (7,80)	
Place where I travel		
La Guaira	1	1,5
Maicao	1	1,5
Mene Grande	1	1,5
Sinamaica	1	1,5
Villa del Rosario	1	1,5
Contact with diphtheria	13	19,4
Origin (Municipality)		
Cabimas	4	6,0
Cañada de Urdaneta	2	3,0
Guajira	2	3,0
Jesús Enrique Losada	3	4,5
Lagunillas	15	22,4
Mara	3	4,5
Maracaibo	31	46,3
Miranda	1	1,5
Rosario de Perijá	2	3,0
San Francisco	3	4,5
Valmore Rodríguez	1	1,5
Education level		
Illiterate	1	1,5
Primary:		
Complete	2	3,0
High school:		
Incomplete	11	16,4
Complete	40	59,7
Technical education:		
Incomplete	2	3,0
Complete	5	7,5
University:		
Incomplete	2	3,0
Complete	4	6,0
Vaccination history		
Complete	4	6,0
Incomplete	5	7,5
Unknown	58	86,6

Table 3. Economic characteristics of the patients.

Current occupation	Frequency	Percentage
Lawyer	1	1,5
Construction worker	1	1,5
Housewife	16	23,9
Pharmacy assistant	1	1,5

Current occupation	Frequency	Percentage
Bionalist	1	1,5
Shrimp	1	1,5
Kangaroo	1	1,5
Businessman	23	34,3
Accountant	1	1,5
Shipper in oil company	1	1,5
Student	12	17,9
Indigent	1	1,5
Nurse	1	1,5
Military	1	1,5
None	1	1,5
Police officer	1	1,5
Fisherman	1	1,5
Secretary	1	1,5
School Transportation	1	1,5
Socioeconomic status (Graffar-Méndez Castellano method)		
Stratum III = middle class	6	9,0
Stratum IV = working class	52	77,6
Stratum V = poverty points	9	13,4

Table 4. Clinical and laboratory characteristics of the patients.

Clinical features		
Time elapsed from the onset of symptoms to hospitalization. (Mean)	1-15 (3,58)	
Form of presentation	Frequency	Percentage
Respiratory	67	100
Clinical presentation		
Tonsillitis	67	100
Clinical manifestations		
Fever	60	89,6
Dysphagia	67	100
Dyspnoea	21	31,3
Presence of adherent pseudomembrane	67	100
Stridor	4	6,0
Bull neck	28	41,8
Received diphtheria antitoxin	25	37,3
Complications		
Severe respiratory insufficiency	10	14,9
Acute Renal Injury	3	4,5
Toxic Cardiomyopathy	3	4,5
Toxic Neuropathy	3	4,5
None	52	77,6
Hospitalization Days (Mean)	0-29 (11,18)	
Laboratory characteristics		
Case confirmed by		
Clinic	52	77,6
Clinical-epidemiological	12	17,9
Laboratory	3	4,5
Egress by		
High medical	45	67,2
Against Medical Opinion	9	13,4
Passed away	13	19,4
fatality rate	13	19,4

5. Discussion

Venezuela from 1992 to 2016 no cases of Diphtheria were reported, so there is currently little epidemiological data on this outbreak. This investigation evaluated the epidemiological characteristics in patients with diphtheria in the Autonomous Service University Hospital of Maracaibo. The incidence of diphtheria was determined, obtaining 25 cases per million inhabitants in the State of Zulia, this is far from that obtained by Garib et al. [6], in the Dominican

Republic that reported the average annual incidence of diphtheria of 4,91 cases per million people from 2000 to 2003, amounted to 8,8 cases per million during the years 2004 and 2005, and decreased to 0,38 from 2006 to 2014; no cases of diphtheria have been reported since 2011. Probably the incidence of this diphtheria outbreak in Venezuela is influenced by the socioeconomic crisis that the country is going through, where there is a deficiency in the health system, as well as a scarce supply of the vaccine in the last 2 decades in this age group.

When classifying patients according to sociodemographic characteristics, a predominance of the female sex and age between 15-65 years was observed, with a mean of 32,16, these results are similar to those obtained by Both et al. [4], in England, this gender imbalance may reflect a lower susceptibility among men vaccinated during military service and / or a higher injury rate in men who later receive the combined diphtheria-tetanus vaccine. Regarding the age group, when the vaccine was introduced to the EPI, a decrease in the incidence was observed in children under 15 years of age and an increase in adolescents and adults, this associated with the progressive deterioration in compliance with the vaccination schedule.

Regarding travel history in the last month, only 5 cases were reported; most deny contact with diphtheria, for which reason no relationship of recent trips and contact with diphtheria was found, these results are opposite to those obtained by Both et al. [4], who refer 7 cases with recent travel history of which 6 had been in a country where diphtheria was endemic. This is because the patients did not have contact with endemic areas; most of the trips were made between municipalities of the Zulia State, except for a single case that traveled to a neighboring country where diphtheria is not endemic. Most of the cases do not know their vaccination history or are incomplete data similar to those obtained by Mahomed et al. [3], where 75% had been incompletely or never immunized, in contrast to that reported by Garib et al. [6], where vaccination coverage reached 89%. This is probably associated with a progressive deterioration in recent years, in the acquisition of vaccines and medicines, as well as electrical failures that compromise the cold chain and the maintenance of vaccines.

The predominant level of education was complete secondary education, however 1,5% are illiterate; the current occupation that prevailed was merchant, followed by housewife and student, the latter in 17,9%, results that contrast with the obtained by Allan et al. [2], in India where 49% were students and 15% of the cases had never attended school. This is influenced by the underdevelopment conditions that the country is going through, where the educational system has also suffered a progressive deterioration with school absences, a decrease in school and university enrollment, as well as a deficit of educators. Regarding the socioeconomic characteristics, it was characterized by the working class, followed by extreme poverty; this is far from the data obtained by Allan et al. [2], where there were no significant differences in socioeconomic

characteristics. Again associated with the country situation, where we observe intense socioeconomic instability, where purchasing power is low, therefore, attendance at hospital centers and the purchase of medicines are difficult.

When describing the clinical characteristics, the respiratory form in its clinical presentation tonsillitis predominated in the 67 cases, this is similar to that reported by Garib et al. [6], where cutaneous diphtheria was not reported, however, it differs from Both et al. [4], where at least 5 of 20 cases were found to have cutaneous diphtheria. The clinical manifestations with fever, dysphagia and the presence of adherent pseudomembrane predominated almost in all cases. These results are corroborated with those obtained by Santos et al. [8], in Brazil and Mahomed et al. [3], in South Africa where the formation of the pseudomembrane in the tonsils is reported as a clinical sign. This coincides with the classic presentation of diphtheria known to date, thus favoring the clinical diagnosis, due to the fact that there is a deficiency in the performance of confirmatory paraclinical studies. Diphtheria if not detected early and treated promptly can cause significant morbidity and mortality due to critical complications, such as acute respiratory failure, acute kidney injury, toxic cardiomyopathy and toxic neuropathy, these reported in 9 cases, in contrast to Santos et al. [8], where they report 4 cases with toxic neuropathy. This is also associated with the inconsistency in the supply of diphtheria antitoxin in the country.

Of a total of 67 cases, 52 were confirmed clinically, while 3 were confirmed by laboratory and 12 clinical-epidemiological, these results differ from those obtained by Santos et al. [8], in Brazil, of which out of 27 cases 9 were confirmed by laboratory, 7 by clinical criteria and 11 by clinical-epidemiological criteria. Although more cases were reported in this study, fewer cases were laboratory confirmed, due to difficulties in processing the samples. The case fatality rate was similar to that obtained by Garib et al. [6] and Mahomed et al. [3], who report rates of 32,5% and 27% respectively and is far from Both et al. [4] which reports a slightly lower rate of 10%. This may be associated with the aforementioned socio-economic crisis, where there is a shortage of medical supplies for care and early detection of the disease.

This study is limited to a single hospital center; the sample did not include patients under 15 years of age. One of the main weaknesses was the processing of laboratory samples.

6. Conclusion

Based on the results, it is concluded that diphtheria is an infectious disease of mandatory notification, reemerging in Venezuela in recent years, currently few data are known on the epidemiological aspects, an incidence of 25 cases per million of inhabitants in the State of Zulia. When classifying the patients according to sociodemographic and economic characteristics, a predominance of the female sex and age between 15-65 years was observed, with a mean of 32,16 years. Regarding travel history in the last month, only 5 cases were reported; most deny contact with diphtheria, for which

reason no relationship of recent trips and contact with diphtheria was found. A high percentage of cases do not know their vaccination history or it is incomplete. The predominant level of education was complete secondary education, however 1,5% are illiterate; the current occupation that prevailed was merchant, followed by housewife and student, the latter by 17,9%. Regarding the socioeconomic characteristics, it was characterized by the working class, followed by extreme poverty. When describing the clinical and laboratory characteristics, the respiratory form in its clinical presentation tonsillitis predominated in 100% of the cases. The clinical manifestations with fever, dysphagia and the presence of adherent pseudomembrane predominated in almost all cases, so this presentation favors the clinical diagnosis of diphtheria. Critical complications should be taken into account, such as acute respiratory failure, acute kidney injury, toxic cardiomyopathy and toxic neuropathy, these reported in 22,4% of cases. Only 4,5% were confirmed by laboratory while most of the cases presented a clinical diagnosis. Diphtheria if not detected early and treated promptly can cause a significant fatality rate of 19,4%, so prevention and control is essential to eradicate the disease.

7. Recommendations

Consequently, it is recommended to increase vaccination coverage in those over 15 years of age and to maintain efficient epidemiological surveillance to reduce the incidence, since diphtheria is a vaccine-preventable disease. Keep health personnel updated on diphtheria care protocols to carry out early detection and timely treatment. Carry out education campaigns to the community for the prevention and promotion of the disease, in this way to raise awareness to have timely care and reduce the rate of fatality.

Acknowledgements

I thank all the people who collaborated in carrying out this research. The study was self-financed. The author declares that he has no conflict of interest.

References

- [1] Parande M., Mantur R., Mantur B., Parande A., & Shinde R. (2017). Resurgence of diphtheria in rural areas of North Karnataka, India. *Indian Journal of Medical Microbiology*, 35, 247-251.
- [2] Allam R., Uthappa C., Duerst R., Sorley E., Udaragudi P., Kampa S., & Dworkin M. (2016). A Case-control Study of Diphtheria in the High Incidence City of Hyderabad, India, *The Pediatric Infectious Disease Journal*, 35 (3): 253-256.
- [3] Mahomed S., Archary M., Mutevedzi P., Mahabeer Y., Govender P., Ntshoe G., Kuhn W., Thomas J., Olowolagba A., Blumberg L., McCarthy K., Mlisana K., Du Plessis M., Von Gottberg A., & Moodley P. (2017). An isolated outbreak of diphtheria in South Africa, 2015, *Epidemiol. Infect.*, 1- 9.

- [4] Both L., Collins S., Zoysa A., White J., Mandal S., & Efstratiou A. (2014). Molecular and epidemiological review of toxigenic diphtheria infections in England between 2007 and 2013. *J. Clin. Microbiol.*, 1- 20.
- [5] Belchior E., Sabine H., Badell E., Collet L., Benoit T., Montera A., Guiso N., Patey O., Levy D., Filleul L., Chieze F., & Olivier S. (2017). Diphtheria in Mayotte, 2007–2015, *Emerging Infectious Diseases*, 23 (7): 1218-1220.
- [6] Garib Z., Danovaro C., Tavaréz Y., Leal I., & Pedreira C. (2015). Diphtheria in the Dominican Republic: reduction of cases following a large outbreak. *Pan-American Journal of Public Health*, 38, 292–299.
- [7] Pan-American Health Organization / World Health Organization. (2018). Epidemiological Update: Diphtheria. February 28. Washington, D.C.
- [8] Santos L., Sant'Anna L., Ramos J., Ladeira E., Stavracakis R., Borges L., Santos C., Napoleão F., Camello T., Pereira G., Hirata J., Vieira V., Cosme L. Sabbadini P., & Mattos A. (2015). Diphtheria outbreak in Maranhão, Brazil: microbiological, clinical and epidemiological aspects. *Epidemiol. Infect.*, 143, 791–798.
- [9] Ministry of Popular Power for Health. (2016). Epidemiological week No. 52 from December 25 to 31, 2016. *Epidemiological Bulletin*, Year of edition LX.
- [10] Guiso N. (2015). Impact of vaccination on epidemiology of diphtheria and pertussis, *Molecular Therapy and Prevention of Human Disease (URE)*, Institut Pasteur, Paris, France. *Vaccine Research*, 2 (1): 6-8.
- [11] Kasper D., Fauci A., Braunwald E., Hauser S., Longo D., Jameson L., & Loscalzo J. (2016). Diphtheria and Other Infections Caused by *Corynebacteria*. *Harrison's Principles of Internal Medicine*; 19th edition; Mexico: McGraw Hill Interamerican, 175, 911-981.
- [12] World Health Organization. (2017). Diphtheria vaccine: WHO position paper - August 2017. *Weekly epidemiological record Relevé épidémiologique hebdomadaire*, 92 (31): 417–436.
- [13] Clarke K. (2016). Review of the epidemiology of diphtheria - 2000-2016. *Us Center for Disease control and prevention*, 1-35.
- [14] Kliegman R., Stanton B., Schor N., Geme J., & Behrman R. (2011). Part XVII Infectious diseases. Diphtheria (*Corynebacterium diphtheriae*). *Nelson Treaty of Pediatrics*, 19th edition. Elsevier; 180, 1-4.
- [15] Núñez L., Córdova J., & González J. (2017). Action protocol for epidemiological surveillance and medical conduct in suspected cases of diphtheria. *Epidemiology Service of the Autonomous Service University Hospital of Maracaibo*, 1 - 31.
- [16] Méndez H. (1986). Social stratification modified Graffar method. *Venezuelan Archive of Childcare and Pediatrics*, 49, 93-104.