Suppurative Meningitis in the Infectious Diseases Clinic - Etiology, Clinic, Laboratory, Course and Outcome

Rron Hoxha [1]

[1] *University of Prishtina "Hasan Prishtina", Faculty of Medicine - General Medicine. rronhoxha94@gmail.com*

KEYWORDS
Suppurative meningitis, Bacterial meningitis, infection, Infectious Diseases Clinic, treatment.

ABSTRACT
Suppurative meningitis is a bacterial infection of the meninges, which are the protective membranes for the brain and spinal cord, resulting in inflammation[1]. Bacterial meningitis is most commonly caused by Streptococcus pneumoniae and Neisseria meningitidis and continues to pose a major public health threat. The morbidity and mortality of meningitis depend on the uncontrolled inflammatory response of the infected person or host [2]. The purpose of this paper is to present the epidemiological, clinical and laboratory features of cases with bacterial meningitis treated at the Infectious Diseases Clinic within the studied period January 2021 – December 2022. To present the impact of the COVID-19 pandemic on the number of cases treated at the Infectious Diseases Clinic in Prishtina, Kosovo. The total number of patients with bacterial meningitis who received treatment at the Infectious Diseases Clinic during the period from January 2021 to December 2022 was 66. The number of cases was much higher in 2022 compared to 2021.

1. Introduction

Suppurative meningitis is a bacterial infection of the meninges, which are the protective membranes for the brain and spinal cord, resulting in inflammation. It is a serious and life-threatening condition that requires immediate diagnosis and treatment [1]. Bacterial meningitis is most commonly caused by Streptococcus pneumoniae and Neisseria meningitidis and continues to pose a major public health threat. The morbidity and mortality of meningitis depend on the uncontrolled inflammatory response of the infected person or host [2]. Acute bacterial meningitis is the most common bacterial infection of the central nervous system (CNS). It is a devastating disease, especially in newborns (age < 1 month) and infants (age < 1 year). Bacterial meningitis has a high fatality rate of up to 30%, and up to 50% of survivors develop neurological complications, which largely depend on the age of the patient and the infecting organism [3].

Bacterial meningitis is a life-threatening infection of the CNS. Bacteria enter the cerebrospinal fluid and subarachnoid space, either by crossing the blood-brain barrier (through the microvasculature of the brain's parenchyma or the cerebrospinal fluid barrier via the choroid plexus or arachnoid microvasculature) or from a nearby infection zone. Pathogen-associated molecular patterns and molecular patterns resulting from damage in the cerebrospinal fluid provoke a massive and often uncontrolled inflammatory response, leading to a high rate of complications, morbidity, and mortality in patients [4, 5].

2. Literature Review

A. Etiology and epidemiology

Suppurative meningitis is caused by bacterial infection of the meninges, resulting in inflammation. The infection can be community-acquired or hospital-acquired. Community-acquired bacterial meningitis results from the invasion of bacteria into the meninges from bacteremia or direct spread from local infection. The bacterial cause varies according to age. Group B Streptococcus is common in infants under 2 months, while Streptococcus pneumoniae is the most common cause in all other age groups, except for ages 11-17, where Neisseria meningitidis remains the most common cause.

Table 1. Common Causes of Meningitis by Age Group

Age Group	Most Common Microorganisms
Neonates (premature birth)	Group B Streptococcus, Escherichia coli
Infants <3 months	Group B Streptococcus, E. coli, S. pneumoniae, L. monocytogenes
Older Children (3 months – 10	S. pneumoniae, N. meningitidis, H. influenzae

years)	
Adolescents (up to 19 years)	N. meningitidis, S. pneumoniae

Other less common causes include Listeria monocytogenes and gram-negative bacteria such as Escherichia coli, Klebsiella, Enterobacter, Pseudomonas aeruginosa. Haemophilus influenzae is still occasionally seen in unvaccinated individuals. Nosocomial infections are caused by S. pneumoniae, Staphylococcus aureus, Staphylococcus albus, and gram-negative bacilli [6, 7].

B. Pathophysiology

To cause meningitis, bacteria must penetrate the meninges through several mechanisms. Bacteremia, or the presence of bacteria in the bloodstream, can result in the crossing of bacteria over the blood-brain barrier. This can only be achieved by certain bacteria, most commonly Neisseria meningitidis and Streptococcus pneumoniae. Bacteria can also directly pass from otitis media or sinusitis into the central nervous system (CNS). Dural defects, either congenital or acquired, allow bacteria to enter the CNS. Hospital-acquired bacterial meningitis results from manipulation of the meninges during neurosurgical procedures.

The invasion of bacteria into the subarachnoid space results in inflammation of the meninges. Although several factors may be involved, lipopolysaccharides in the walls of gram-negative organisms and teichoic acid in the walls of gram-positive organisms activate microglia in the brain, leading to a cascade of inflammatory changes that cause cortical microvascular permeability with diffuse cerebral edema, resulting in increased intracranial pressure. This causes the patient to experience headache and fever. Disruption of the blood-brain barrier occurs as a secondary consequence of infection and the inflammatory response. Altered mental status, seizures, and focal neurological deficits occur due to decreased perfusion and increased intracranial pressure [8].

Meningitis develops when the pathogen invades the CNS either via the hematogenous route (bacteremia) or by direct spread secondary to sinusitis or mastoiditis, and multiplies in the subarachnoid space. The presence of bacteria in the subarachnoid space leads to the activation of the immune response, resulting in bacterial lysis. The presence of bacterial particles triggers a further inflammatory response with the continuous migration of neutrophils across the blood-brain barrier and the sustained release of cytokines and chemokines (including IL-1B or CXCL1,2,5). This ongoing inflammatory state then leads to decreased cerebral perfusion, cerebral edema, increased intracranial pressure, metabolic disturbances, and vasculitis, all contributing to neuronal damage and ischemia [8].

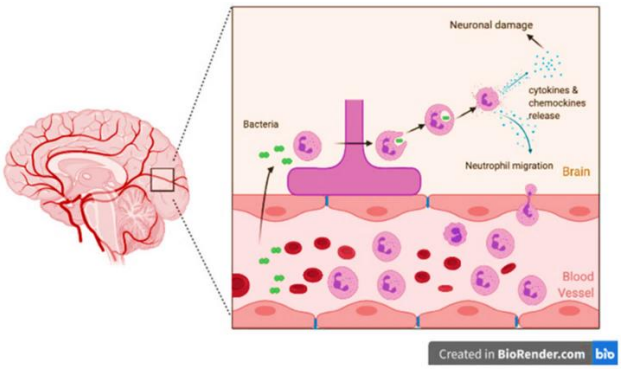

Figure 1 illustrates the pathophysiology of neuronal damage in bacterial meningitis [8].

C. Clinical manifestations

The early clinical signs of bacterial meningitis are nonspecific and include fever, fatigue, and headache, followed by meningism (neck stiffness), photophobia, phonophobia, and vomiting, which develop due to meningeal irritation [9].

Headache and neck stiffness indicate inflammatory activation of trigeminal sensory nerve fibers in the meninges, which can be blocked experimentally by 5-HT1B/D/F receptor agonists (triptans) [10].

Fever, neck stiffness, and altered mental status form the classic triad of symptoms for meningitis. However, this triad is present in only 41% of bacterial meningitis cases. It is more commonly observed in elderly patients. Seventy percent of patients present with at least one of these symptoms. Early common symptoms include fever, headache, and confusion, which can progress to stupor, focal neurological deficits, and seizures. The history

should include questions about any recent neurosurgical procedures, immunization status, and lifestyle. Physical examination may reveal nuchal rigidity or positive Kernig or Brudzinski signs. However, their absence does not reliably exclude the disease. Brudzinski's sign occurs when passive neck flexion causes involuntary knee flexion. Kernig's sign is resistance or pain with knee extension when the patient is lying supine and the thigh is flexed at 90 degrees. These signs are thought to be secondary to meningeal irritation. Fundoscopic examination may reveal papilledema due to increased intracranial pressure. A rapidly spreading petechial rash, known as purpura fulminans, may suggest meningococcal infection [8].

It is important to note that the classic triad of fever, neck stiffness, and altered mental state is present in less than 50% of adults with proven bacterial meningitis [7].

Infants may present with a range of nonspecific symptoms, including lethargy, irritability, and, in some cases, bulging fontanelles. Older children and adults typically present with headache, fever, photophobia, vomiting, neck stiffness, and altered mental status. Meningococcal disease often presents with a petechial rash on the lower extremities, which appears after the initial nonspecific symptoms, although this symptom may also be present in pneumococcal meningitis [9].

D. Diagnosis, Treatment and Prognosis

Patients suspected of having bacterial meningitis should undergo a lumbar puncture to obtain a sample of cerebrospinal fluid (CSF). The cerebrospinal fluid should be sent for Gram staining, culture, complete blood cell count (CBC), and determination of glucose and protein levels. Bacterial meningitis usually results in low glucose levels and high protein levels in the cerebrospinal fluid. Since CSF glucose levels depend on blood glucose levels, the ratio of CSF glucose to serum glucose is considered a more reliable parameter for diagnosing acute bacterial meningitis than absolute CSF glucose levels. A predominance of neutrophils is expected in the cell count [10].

The diagnosis can be confirmed by identifying bacteria through Gram staining or culture. A non-contrast CT scan of the head should be performed before lumbar puncture if the patient is at risk of herniation. Risk factors for herniation include papilledema seen on examination, seizures, focal neurological deficits, or if the patient is immunocompromised. Lumbar puncture should be delayed if the patient has unstable vital signs, coagulation abnormalities, or has had recent seizures. Empiric antibiotic therapy is recommended if testing is delayed. Blood cultures should also be taken, as 53% of patients have concurrent bacteremia. Elevated levels of C-reactive protein or procalcitonin suggest a bacterial rather than viral etiology [10, 7].

CSF in bacterial meningitis is characterized by a very high white blood cell count (<500 cells/µl) with a predominance of neutrophils and significantly elevated protein levels (<1 g/l), indicating severe damage to the blood-CSF barrier. Elevated lactate (<0.3g/l) and a decreased CSF/blood glucose ratio (>0.4) support the diagnosis of acute bacterial meningitis [8].

Peripheral blood white cells, erythrocyte sedimentation rate, serum C-reactive protein, procalcitonin, and other acute phase proteins are usually elevated in bacterial meningitis but have limited diagnostic value, particularly in atypical cases. Moreover, typical CSF findings mentioned above may differ in the early stages of the disease and in patients who have been inadequately treated with antibiotics .

A head CT provides information about intracranial complications such as brain edema, hydrocephalus, and infarctions. In addition, bone imaging from the CT can identify parameningeal foci such as sinusitis, mastoiditis, or odontogenic abscess. Local infections are especially common in pneumococcal meningitis and may require surgical treatment [30]. Treatment consists of the use of antimicrobial therapy, supportive therapy, replacement therapy, symptomatic therapy, and correction of increased intracranial pressure.

Timely administration of antibiotics is essential. Delays in administration of 3 to 6 hours are associated with increased mortality. The identified bacteria determine the selection of antibiotics. Empirical treatment with ceftriaxone and vancomycin should be considered in cases of diagnostic delay. Immunocompromised patients or those over 50 years of age should also receive ampicillin. Patients with bacterial meningitis due to head trauma or post-neurosurgical procedures should be covered for methicillin-resistant Staphylococcus aureus (MRSA) and aerobic gram-negative organisms. These patients should receive vancomycin and ceftazidime or cefepime. Dexamethasone may increase survival if administered at the same time as antibiotics in Streptococcus pneumoniae infections. It has not been shown to improve outcomes for meningitis caused by other bacteria.

Patients suspected of having meningococcal meningitis should be placed in isolation precautions until 24 hours

after receiving antibiotics. Close contacts should also receive prophylactic treatment, using ciprofloxacin, rifampin, or ceftriaxone. Individuals exposed to the patient's oral secretions during this time should also be treated.

Table 2: Empirical Antibiotic Therapy

	Probable pathogens	Empirical therapy
Neonates	*Gram – negative enterobacteriacae (e.coli, klebsiella, enterobacter. proteus, Gr.B streptococci*	*Cephalosporin + Ampicilin*
Infants and children	*N.meningitides, S.pneumoniae (Haemophilus influenza)*	*Cephalosporin (Vancomycin or Rifampin)*
Adults	*S.pneumoniae, N.meningitidis, L.monocytogenes, Aerobic streptococci*	*Cephalosporin (+Ampicilin)*
Nosocomial, trauma, ventriculitis, shunt infection	*Staphylococci, Gr-negative, Enterobacteriacae, P. aeruginosa*	*Meropenem or Cephalosporin + Vancomycin (or Rifampicin, Fosfomycin, Linezolid)*
Immunocompromised patients	*L.monocytogenes, Gr – enterobacteriacae, S.pneumoniae, P.aeruginosa*	*Cephalosporin + Ampicilin(+ Vancomycin)*
Resource – limited countries	*N.meningitidis, S.pneumoniae, H.influenzae, L.monocytogenes*	*Ceftriaxone, Chloramphenicol, Penicilin G, Ampicilin/ Amoxicilin*

The mortality rate for bacterial meningitis varies between 10-15%. Survival depends on early recognition of acute bacterial meningitis, followed by the administration of appropriate antibiotic therapy. Delays in treatment can result in increased intracranial pressure, causing decreased cerebral perfusion, which can quickly lead to unconsciousness and death [7].

E. Complications

Bacterial meningitis can have a typical course but can often be complicated, depending on many factors [10]. Several complications are associated with bacterial meningitis. These include short-term complications such as seizures, focal neurological deficits, and subdural effusions, as well as long-term complications such as hearing loss, cognitive impairments, hydrocephalus, learning disabilities, and epilepsy.

1. Subdural effusion and empyema

Subdural effusion refers to the pathological accumulation of fluid in the dura mater. It is common in young children and infants, but after the age of 2, it becomes very rare [10].

2. Focal neurological deficits

Focal neurological deficit refers to a range of signs and symptoms resulting from a lesion localized to a specific anatomical site in the central nervous system.

3. Hearing loss

Sensorineural hearing loss is the most common neurological consequence of bacterial meningitis. Hearing loss can develop either as a direct spread of bacterial products or as a result of the host's inflammatory response in the meninges and CSF.

4. Cognitive impairments

Due to irreversible neuronal damage occurring during bacterial meningitis, there is a significant risk of developing long-term cognitive deficits and learning difficulties. [8].

5. Seizures and epilepsy

Seizures are one of the clinical presentations of bacterial meningitis [6]. In cases of bacterial meningitis with seizures, if the seizures develop early in the illness and are easily controlled, permanent neurological complications are rarely a concern. [6].

6. Hydrocephalus

Hydrocephalus appears as a late complication of bacterial meningitis in the second or third week of the disease, resulting from obstruction to the free circulation of CSF, either intraventricular due to ventriculitis or extraventricular due to arachnoiditis [6].

F. Prevention

Vaccines are available to help prevent bacterial meningitis. Children can receive a meningitis vaccine around the age of 11 to 12 years, followed by a booster vaccine at age 16. Bacterial meningitis is most common in infants under 1 year of age and in young people aged 16 to 21. College students living in dormitories or other close environments are at increased risk. In addition, adults with compromised immune systems, such as post-splenectomy individuals, are at higher risk [7].

The most effective prevention of neurological complications from bacterial meningitis is preventing the infection through infant and childhood vaccination programs. Despite the development of several vaccines against organisms that cause bacterial meningitis, there continue to be many outbreaks caused by vaccine-preventable microorganisms .

Currently, vaccines are available against three organisms that cause bacterial meningitis: Hib (Haemophilus influenzae type b), Neisseria meningitidis (capsular groups A, B, C, W, and Y), and 23 of the more than 90 serotypes of Streptococcus pneumoniae. The conjugate Hib vaccine targets only Haemophilus influenzae type b and is administered in three or four doses before the age of 18 months. There are two types of vaccines against Neisseria meningitidis: conjugate vaccines against capsular groups A, C, W, and Y, and protein-based vaccines against group B. There are also two types of vaccines against S. pneumoniae: conjugate pneumococcal vaccines (PCV 10 against 10 serotypes, PCV 13 against 13 serotypes) and polysaccharide vaccines against 23 serotypes, which are not routinely used in healthy children.

Routine vaccination can lead to the development of herd immunity, indirectly preventing transmission within a population.

G. Impact of the COVID-19 Pandemic

The first case of infection with SARS-CoV-2 was isolated in December 2019 in Wuhan, China [45]. Since then, the number of infected individuals has increased significantly. According to the World Health Organization (WHO), the number of people infected as of October 6, 2021, exceeded 235 million, while the death toll was around 4.81 million [46].

In addition to the high number of infections and deaths, the COVID-19 pandemic has significantly affected the quality of medical services for patients with other diseases, including bacterial meningitis patients. In most countries worldwide, movement restrictions both within and outside the country were implemented, making access to healthcare difficult. In high-income countries, healthcare continuity was maintained by utilizing telemedicine services, allowing patients to continue accessing healthcare remotely to some extent. However, in low- and middle-income countries, including Kosovo, such services were not feasible, and the pandemic's impact was more significant.

3. Motivation and Objectives

The purpose of this study is to present the epidemiological, clinical, and laboratory characteristics of cases of bacterial meningitis treated at the Infectious Diseases Clinic during the study period. Additionally, the study aims to present the impact of the COVID-19 pandemic on the number of cases treated at the Infectious Diseases Clinic in Prishtina, as well as the pandemic’s impact on other healthcare services provided to non-COVID patients.

4. Methodology

This is a cohort study conducted in a single center, observational and retrospective in nature. Demographic, clinical, laboratory, and biochemical data, as well as treatment methods, disease progression, and outcomes, were collected retrospectively from 66 patients hospitalized at the Infectious Diseases Clinic in Prishtina with bacterial meningitis during the years 2021 and 2022.

The statistical analysis of the data was conducted using IBM SPSS Statistics Version 26, and results were

presented in Microsoft Word through relevant tables and graphs. The following statistical parameters were calculated: frequency, arithmetic mean, minimum, maximum, and standard deviation (SD). The difference between groups was evaluated using the One-way ANOVA test. A p-value less than 0.05 was considered statistically significant.

5. Results

The total number of patients with bacterial meningitis who received treatment at the Infectious Diseases Clinic from January 2021 to December 2022 was 66. The number of patients was significantly higher in 2022 compared to 2021. In 2022, there were a total of 65 patients, or 98.5%, while in 2021, there was only 1 patient, or 1.5%. Out of a total of 66 patients, 24 (36.4%) were female, and 42 (63.6%) were male.

Table 3. Number of cases distributed during the period January 2021 – December 2022

Year	Number of Cases	Percentage
2021	1	1.5%
2022	65	98.5%
Total	66	100%

Table 4. Number of cases from January 2021 - December 2022 distributed by gender

Gender	Number	Percentage
Female	24	36.4%
Male	42	63.6%
Total	66	100%

Regarding the number of cases by month during the period January 2021 - December 2022 that required treatment at the Infectious Diseases Clinic due to bacterial meningitis, it was found that in March and May, the frequency of cases was highest, with 11 cases each month, or (16.7% for each month). In June, there were 9 cases or (13.6%), in February 8 cases or (12.1%), in January, April, and July there were 5 cases each month or (7.6% for each month), in October there were 4 cases or (6.1%), in September and December there were 3 cases each or (4.5% each), and in August, there were only 2 cases or (3.0%), while in November 2019, no cases were admitted to the Infectious Diseases Clinic (Table 5).

Table 5. Statistical data (average, minimum value, maximum value, and standard deviation) for the age of patients during the period January 2021 - December 2022

Number of Patients	66
Average	21.30
Maximum Value	75
Minimum Value	1
Standard Deviation	22.407

From Table 5, we see that during the period January 2021 - December 2022, the average age of patients was 21.30 (min 1 - max 75 with SD 22.407).

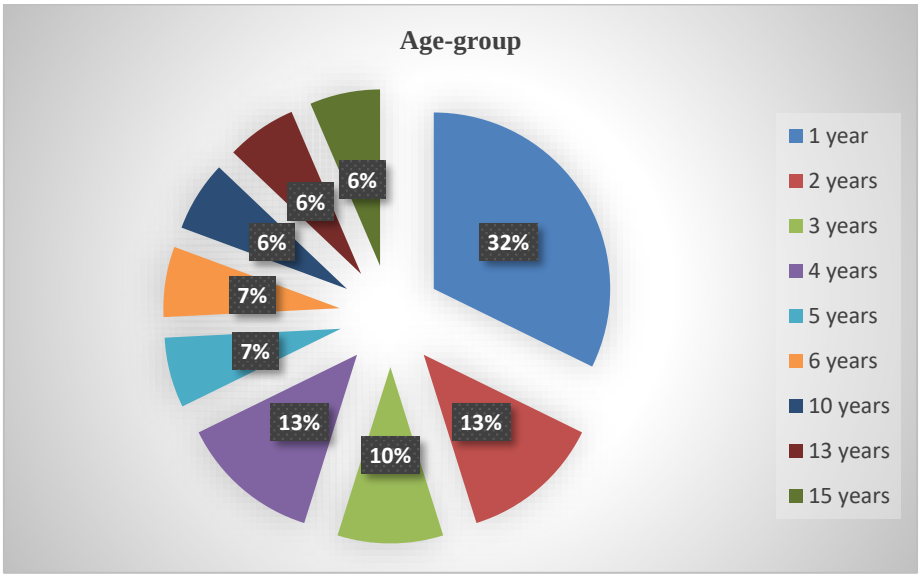

Diagram 1. Most common cases of bacterial meningitis by age group

Out of a total of 66 cases during this period, the predominant age groups were young children up to 10 years, with 10 cases at the age of 1 year, 4 cases each at the ages of 2 and 12 years, 3 cases at the age of 3 years, 4 cases at the age of 4 years, while the age groups of 5, 6, 10, 13, and 15 years each had 2 cases. Other age groups were represented by 1 case each (Diagram 1).

Table 6. Statistical data (average, minimum value, maximum value, and standard deviation) for the onset of the disease prior to hospitalization (in days) for the period January 2021 – December 2022

Number of Patients	**66**
Average	4.30
Minimum Value	0
Maximum Value	60
Standard Deviation	7.813

Regarding the onset of the disease prior to hospitalization (in days), we can say that the average for the period January 2021 - December 2022 for 66 patients with bacterial meningitis was 4.30 (min 0 – max 60, SD 7.813). We can say that in most of these cases, the disease had a short development course (average of 4 days before hospitalization), which indicates the acute progression of the disease (Table 6).

In 7 cases, or (11%), the disease started on the same day as hospitalization, in 17 cases or (26%) it started 1 day before hospitalization, in 13 cases or (20%) it started 2 days before hospitalization, in 7 cases or (11%) it started 5 days before hospitalization, in 5 cases or (8%) it started 3 days before hospitalization, in 4 cases or (6%) it started 7 days before hospitalization, in 4 cases or (6%) it started 14 days before hospitalization, while in 3 other cases or (1% each), the disease started 60, 11, and 8 days before hospitalization.

The average length of hospitalization for the period January 2021 – December 2022 was 26.24 days (min 1 – max 155, SD 25.154) (Table 7).

Table 7. Duration of hospitalization expressed in days for the period January 2021 - December 2022

Number of Patients	**66**
Average	26.24
Minimum Value	1
Maximum Value	155
Standard Deviation	25.154

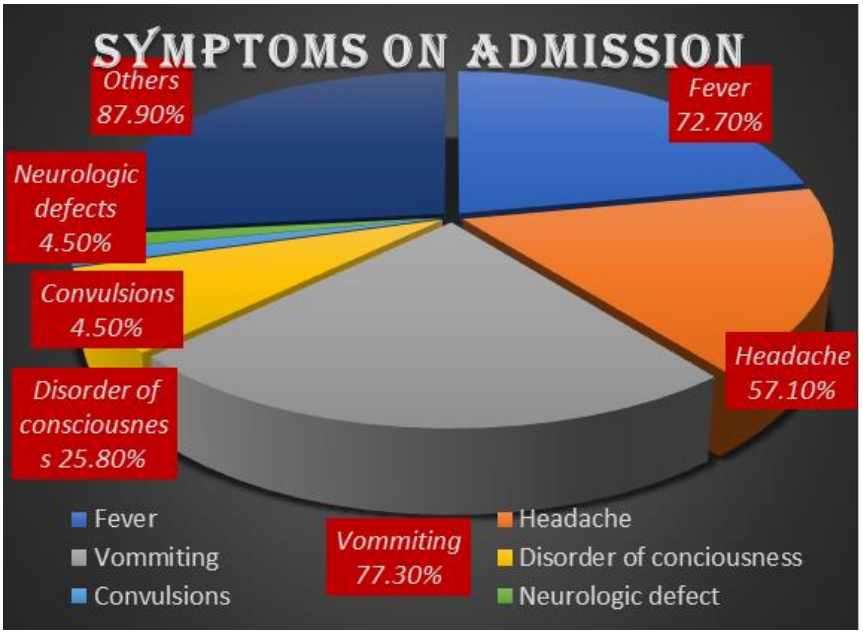

Diagram 2. Presentation of the percentage of symptoms upon admission of patients with bacterial meningitis for the period January 2021 - December 2022

Upon admission to the Infectious Diseases Clinic of patients with bacterial meningitis during the period January 2021 – December 2022, it was observed that in 48 cases or 72.70%, fever was present, in 37 cases or 57.1%, headache, in 51 cases or 77.3%, vomiting, in 17 cases or 25.8%, altered consciousness, in 3 cases or 4.5%, seizures, also in 3 cases or 4.5%, neurological deficits, and in 58 cases or 87.9%, other symptoms were present upon admission. Thus, it is evident that the predominant symptoms were vomiting, fever, and headache.

Table 8. Statistical data (average, minimum value, maximum value, and standard deviation) regarding the laboratory data for patients admitted with bacterial meningitis during the period January 2021 – December 2022

Laboratory Data	Average	Minimum Value	Maximum Value	Standard Deviation
Leukocytes (number)	13.76	1	30	6.819
Neutrophils (%)	74.15	26	97	17.127
CRP	81.29	0	378	86.90
Procalcitonin	9.65	0	100	22.366
CSF – cellular elements (number)	690.48	10	4522	780.19
CSF – cellular elements PMN% - p%	43.26	10	90	24.075
CSF – cellular elements PMN% - M%	63.53	10	100	27.190
CSF – biochemistry – glucose	3.06	0	20	2.938
CSF – biochemistry – protein	1.72	0	5	1.228

Regarding the laboratory data concerning patients admitted to the Infectious Diseases Clinic during the period January 2021 – December 2022, it can be said that leukocytes upon admission for the samples of 66 patients had an average of 13.76 (min 1 – max 30, SD 6.819), neutrophils had an average of 74.15 (min 26 – max 97, SD 17.127). CRP determined in 48 cases had an average of 81.29 (min 0 – max 378, SD 86.90), procalcitonin

determined in 20 cases had an average of 9.65 (min 0 – max 100, SD 22.366), cellular elements in number in the cerebrospinal fluid with an average of 690.48 (min 10 – max 4522, SD 780.19), cellular elements in the form of polymorphonuclear (in this case P) in the cerebrospinal fluid determined in 43 cases with an average of 43.26 (min 10 – max 90, SD 24.075), cellular elements of polymorphonuclear (in this case M) in the cerebrospinal fluid determined in 51 cases with an average of 63.53 (min 10 – max 100, SD 27.190), glucose determined in the cerebrospinal fluid in 64 cases with an average of 3.06 (min 0 – max 20, SD 2.938) and proteinorrhagia determined in 64 cases with an average of 1.72 (min 0 – max 5, SD 1.228) (table 8).

Table 9. Tabular representation of the bacteriological culture of cerebrospinal fluid taken from samples of patients with bacterial meningitis admitted to the Infectious Diseases Clinic during the period January 2021 – December 2022

BACTERIOLOGICAL ANALYSIS OF CSF	POSITIVE	NEGATIVE	TOTAL	PERCENTAGE
DIRECT MICROSCOPIC PREPARATION	6	16	22	P 9.1%
	N 24.2%			
CSF CULTURE	7	20	27	P 10.6%
	N 30.3%			

The direct microscopic preparation was determined in 22 cases (out of 66 total cases), where 6 or 9.1% of the samples taken were positive, while 16 or 24.2% of the samples were negative. Additionally, bacterial culture was determined in 27 cases out of 66 total cases, where 7 or 10.6% of the samples taken were positive, while 20 or 30.3% of the cases were negative (Table 9).

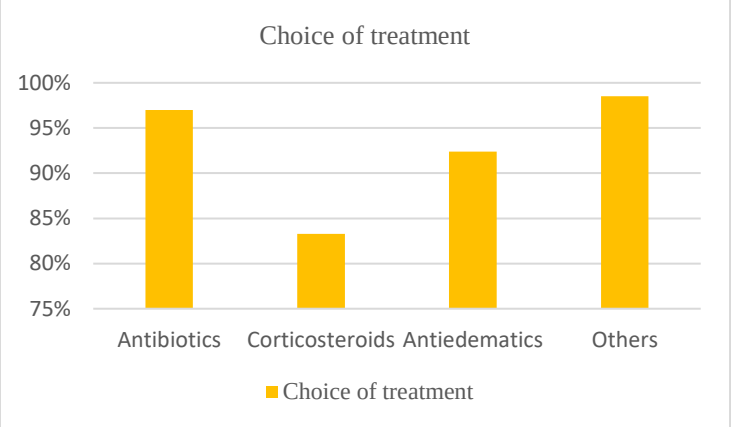

Diagram 3. Treatment and its types used in the treatment of patients with bacterial meningitis at the Infectious Diseases Clinic during the period January 2021 – December 2022

Antibiotic treatment was applied in 64 cases or 97.0% of cases with bacterial meningitis admitted to the Infectious Diseases Clinic during the period January 2021 – December 2022. In 55 cases or 83.3% of cases, corticosteroid treatment was applied. Anti-edema treatment was applied in 61 cases or 92.4%, while other treatments were applied in 65 cases or 98.5% of cases (Diagram 3).

Table 10. Most Common Types of Antibiotics Used in the Treatment of Patients with Bacterial Meningitis at the Infectious Diseases Clinic for the Period January 2021 – December 2022

Antibiotics Used	Cases and % of Use	Cases and % of Non-Use
Penicillins	4 cases	6.1%
Cephalosporins	60 cases	90.9%
Other Antibiotics	41 cases	62.1%

The most commonly used antibiotics in the treatment of patients with bacterial meningitis admitted to the Infectious Diseases Clinic for the period January 2021 – December 2022 were cephalosporins, used in 60 cases

or 90.9%, followed by other antibiotics in 41 cases or 62.1%, and penicillins as the least used antibiotics in only 4 cases or 6.1% (Table 10).

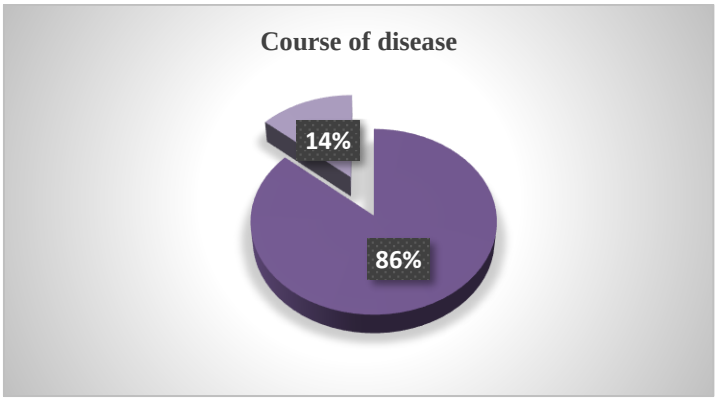

Diagram 4. Course of the disease in patients admitted with bacterial meningitis at the Infectious Diseases Clinic for the period January 2021 – December 2022

Out of a total of 66 hospitalized cases with bacterial meningitis at the Infectious Diseases Clinic for the period January 2021 – December 2022, it was found that in 57 cases or 86% the course of the disease was moderately severe, while in 7 cases or 14% the course of the disease was severe, and in these cases, it ended with exitus (death). It should also be noted that 2 cases were referred for treatment abroad (Diagram 4).

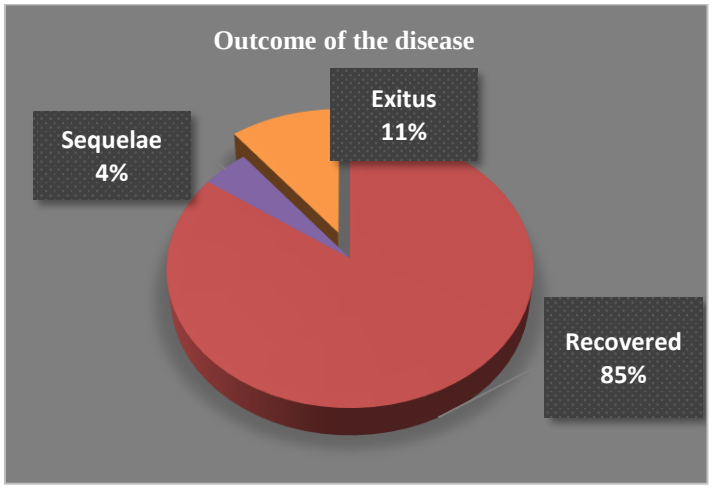

Diagram 5. Outcome of the disease in patients admitted with bacterial meningitis at the Infectious Diseases Clinic for the period January 2021 – December 2022

Regarding the outcome of the disease, it is observed that in 56 cases or 85%, patients fully recovered from the disease, in 3 cases or 4% the disease ended with sequelae, and in 7 cases or 11% the disease ended with exitus (death) (Diagram 5).

The comparison of the two groups using the One-Way ANOVA test is not statistically significant due to the small number of cases in 2021, but it is presented to show the method of comparing epidemiological, clinical, laboratory characteristics, the course of the disease, and its outcome between the two studied groups.

6. Discussion

Based on this research conducted at the Infectious Diseases Clinic during the period from January 2021 to December 2022, we have obtained data regarding the total number of patients with bacterial meningitis, the demographic structure of the patients by age and gender, the most common months, the onset of the disease in days prior to hospitalization, days of hospitalization, clinical signs upon admission, laboratory data at the time of admission, determination of the bacterial culture of cerebrospinal fluid, types of treatments in general and antibiotics in particular, the course of the disease, and its outcome.

It is evident that the number of cases of bacterial meningitis in 2022 was significantly higher (65 cases) compared to 2021 (only 1 case). This difference was high because during the first three quarters of 2021, all

capacities of the Infectious Diseases Clinic were used to treat patients infected with SARS-CoV-2.

The COVID-19 pandemic has brought significant changes to society, from global efforts and specific actions by various countries to control the respiratory spread of the virus (masks, social distancing, quarantine, and lockdown measures) to the restructuring of healthcare systems. The mobilization against the pandemic has affected monitoring, diagnosing, and vaccination programs for a number of vaccine-preventable diseases, including invasive meningococcal disease and meningitis.

The 4th meeting of the Global Meningococcal Initiative (GMI) aimed to: (i) highlight the impact of the COVID-19 pandemic and the lockdown period on the epidemiology and vaccination schedules of meningococcal disease; (ii) highlight the increasing trend of meningitis resistance to antibiotic treatments; and (iii) explore the future of broadly covering meningococcal vaccines.

In our study, there was a significant decrease in cases of bacterial meningitis treated at the Infectious Diseases Clinic in 2021. Notably, after the first case of COVID-19 appeared in March 2020, no patients with bacterial meningitis were admitted. Considering the same period as the previous year, that is, the first quarter of 2022, 24 cases were admitted compared to just one case in 2021. Meanwhile, for the second and third quarters of 2022, 45 cases were admitted compared to the same period in 2021, when no cases of bacterial meningitis were reported.

Since the appearance of the first case of COVID-19, the entire focus of the Infectious Diseases Clinic has been on treating patients infected with the SARS-CoV-2 virus, and we do not have data regarding cases of bacterial meningitis that required hospitalization during that period. Consequently, it is unclear what happened to patients needing treatment for bacterial meningitis during that time; they may have ended up in other clinics of the University Clinical Center or private facilities, but this remains speculative.

A similar situation is observed in other countries, such as France, where there was a significant decrease in cases of bacterial meningitis, especially during the period from March 16 to May 15, 2020, with a total of 23 cases compared to the same period in 2018 (78 cases) and 2019 (68 cases). The reduction in cases in 2020 occurred due to the implementation of strict COVID-19 control measures and lockdowns. Furthermore, the lockdown measures may have affected the transmission of hyper-invasive isolates associated with specific meningococcal serogroups in France.

In particular, cases related to serogroup W (clonal complex: CC11) were high in early 2020 before the implementation of movement restrictions, but during the initial movement restrictions, cases associated with this serogroup decreased significantly (3 cases compared to 14 and 21 cases in the same periods in 2018 and 2019). Despite the reduction in cases with hyper-invasive isolates, there was an indication that in 2020, SARS-CoV-2 infections preceded some cases of bacterial meningitis (n = 4), particularly in the elderly (average age 71 years). However, no confirmatory SARS-CoV-2 tests were available for these cases.

Decreases in meningitis cases during 2021 were also observed in other regions. In Brazil, the number of confirmed cases of bacterial meningitis in 2021 was 357 compared to 1,021 cases in 2022 and 1,131 cases in 2019 (a 65% decrease in the number of cases from 2019). In Chile, there was a 90% reduction in meningitis cases in 2021 compared to 2022. A similar pattern was observed in Mexico, with only 12 reported cases of bacterial meningitis in 2021 compared to 48 cases in 2022.

There was also a significant decrease in cases in South Africa, where there were 111 cases in 2022 compared to 46 cases in 2021.

A marked decrease in bacterial meningitis cases was also observed in China. The incidence rate of bacterial meningitis in 2021 was down by 58% compared to the average incidence rate between 2017 and 2019 (the number of cases in 2021 was 53, while the number in 2019 was 132). A similar trend was observed in Russia, with the incidence rate of bacterial meningitis decreasing by over 50% between 2021 and 2022 (respectively 0.6 and 0.26 cases per 100,000).

Since bacterial meningitis is a well-known disease in many countries and is quite severe, usually requiring hospitalization, it is unlikely that weak monitoring and care by healthcare personnel caused the decline in bacterial meningitis cases in 2021. This is particularly improbable in developed countries where monitoring of bacterial meningitis is at a high level. In general, the data suggest that the reduction in cases of bacterial meningitis was more likely a result of COVID-19 control measures.

In our study, the highest incidence was found in males, with 63.6% of patients being male and 36.4% being female over this two-year period.

Also, regarding the average age of hospitalized patients with bacterial meningitis during this two-year period, it was 21.3, indicating a predominance of the disease in younger populations. The most affected age group identified in this research was 1-10 years old, while the least affected age group was 63-75 years.

Based on our research, the disease had a rapid course of development, with an average of 4 days from the onset of the disease before hospitalization, describing a quite acute progression of bacterial meningitis. Regarding the days of hospitalization, we can say that the average length of stay in the clinic for patients with bacterial meningitis during this two-year period was 26 days.

Clinically, in this study, symptoms such as fever, vomiting, and headache predominated, while disturbances of consciousness, seizures, and neurological defects appeared less frequently. These data obtained from our research align with data found in a study conducted with hospitalized children at Kilifi County Hospital in Kenya. Of the 98 cases in that study, 88 presented with fever, 41 with seizures (out of 98), and 35 with consciousness disturbances (out of 98).

This research also includes the diagnosis of bacterial meningitis determined through laboratory analyses obtained from cerebrospinal fluid and blood samples. Additionally, direct microscopic determination was used, which was determined in 22 out of 66 total cases, resulting positive in only 6 cases. The determination of culture in cerebrospinal fluid was used, which was determined in 27 cases out of 66 total cases, resulting positive in only 7 cases. The data obtained from our study align with the data from this research.

When describing the types of treatments used for patients with meningitis during the period from January 2021 to December 2022, we refer to 4 types of treatments, where antibiotics as first-line drugs were used in 64 cases, corticosteroids in 55 cases, anti-edema drugs in 61 cases, and other medications in 65 cases. Thus, each of these drug groups was used in the majority of patients with bacterial meningitis.

Regarding the types of antibiotics used, the cephalosporin group was the most commonly used antibiotic in a total of 60 cases of bacterial meningitis out of 66 total cases, followed by other antibiotics used in 41 cases, and finally, the penicillin group used in only 4 cases. Therefore, it appears that the most successful group of antibiotics in treating bacterial meningitis was cephalosporins.

In this study, the course and outcome of the disease were also investigated. In 57 cases, the course of the disease was moderately severe, while in 7 cases, it was severe, resulting in death; due to multiple complications associated with the disease, 2 cases were sent for treatment abroad. Additionally, out of 66 total cases, 57 of them resulted in complete recovery, 2 with sequelae, and 7 with exitus (death).

7. Conclusion

Based on the results of this study, we can conclude that:

- The total number of patients with bacterial meningitis who received care at the Infectious Diseases Clinic from January 2021 to December 2022 was 66.
- The number of cases in 2021 (1 patient) was significantly lower compared to 2022 (65 patients).
- The most common months for the appearance of cases were March and May, with 11 cases each (only for 2022).
- The majority of patients (63.6%) were male, while 36.4% were female.
- The average age of hospitalized patients with bacterial meningitis during the period from January 2021 to December 2022 was 21.3 years.
- The most affected age group was 1 to 10 years old, while the least affected age group was 64 to 75 years old.
- The average onset of the disease before hospitalization (in days) was 4.3 days.
- The average length of hospitalization for patients with bacterial meningitis was 26.24 days.
- The dominant symptoms upon admission were: fever (present in 48 cases), vomiting (51 cases), and headache (37 cases).

- Diagnosis was determined through laboratory data obtained from cerebrospinal fluid and blood samples.
- The direct microscopic preparation was positive in 6 cases, while the cerebrospinal fluid culture was positive in 7 cases.
- Treatment for meningitis involved 4 groups of medications: antibiotics in 64 cases, corticosteroids in 55 cases, antiedematous agents in 61 cases, and other medications in 65 cases.
- The most commonly used type of antibiotic was the group of cephalosporins (60 cases), followed by other antibiotics (41 cases) and penicillins (4 cases).
- The course of the disease was moderately severe in 57 cases, while in 7 cases, it was severe.
- In 56 cases (84%), the disease ended with complete recovery, in 3 cases (4%) it ended with sequelae, and in 7 cases (11%) it ended with exitus (death).

These results provide a clear overview of the situation regarding bacterial meningitis during the study period and highlight the importance of monitoring and managing the disease, especially in the context of the impacts that the COVID-19 pandemic had on healthcare services.

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