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Identified Bacteria and Virus in the Cerebrospinal Fluid of under Five Years Hospitalized Children for Clinical Meningitis at Panzi Hospital in the Eastern Part of DRC

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Abstract

Background: Meningitis remains a leading cause of death among children below 5 years of age in the Democratic Republic of the Congo (DR Congo). Distinguishing children with bacterial meningitis from those with viral meningitis in the emergency department is sometimes difficult. Here we identified bacteria and virus in the cerebral spinal fluid (CSF) of children with meningitis. **Material and Methods:** This is a prospective, analytical study carried out in the Pediatrics department of Panzi Hospital in the South-Kivu province of DR Congo. Between April 2021 and March 2022, 150 of 251 collected CSF from children aged from 1 to 59 months hospitalised due to clinical meningitis at Panzi referral university hospital, Bukavu, Eastern DR Congo were sent to the Lancet laboratory for bacteria identification by a multiplex real-time PCR assay for detection of the most different viruses and bacterial species causing meningitis. **Result:** The used multiplex real-time PCR assay allowed us to identify germs in 24.7% of cases (37/150). We isolated bacteria in 25/37 (67.5%) cases, and viruses in 9/37 (24.3%) while virus and bacteria co-infection was detected in 3/37 (8.1%). The most frequently identified bacteria were *Streptococcus pneumoniae* 14/37 (37.8%) followed by *Haemophilus influenzae* 6/37 (16.2%). The main virus was cytomegalovirus 5/37 (3.5%). Despite the age, the most found bacterial are common in children from rural areas and unvaccinated children. Bacterial and virus co-infection were identi-

fied in 66.7% of children aged between 25 - 60 months, mainly among male children, and in all children from rural areas (100%). The overall case fatality rate was 30% and was very high among cases with co-infection CMV-Pneumococcal (66.7%), followed by Streptococcus *pneumoniae* (50%). **Conclusion:** Meningitis remains frequent among children aged from one to 59 months among Bukavu Infants. We noticed that, Children with co-infection with bacteria and viruses might need higher attention when having meningitis symptoms, as this could lead to fatal outcomes. The introduction of molecular techniques, such as multiplex real-time PCR, has the potential to improve diagnosis and patient outcomes.

Keywords

Children, Meningitis, Multiplex Real-Time PCR Meningitis Assay Bacteria, Virus

1. Introduction

The term meningitis means *stricto sensu*: inflammation of the meninges [1].

Bacterial meningitis is an inflammation of the meninges caused by bacteria [2]. In the past decades the epidemiology and treatment strategies for bacterial meningitis have significantly change. The introduction of conjugate vaccines has resulted in reduction of *Haemophilus influenzae* type b, while conjugate pneumococcal and meningococcal vaccines have significantly reduced the burden of bacterial meningitis [2].

The etiologies of meningitis are therefore multiple, but above all infectious, bacterial and viral. Common etiologies of bacterial meningitis are *Haemophilus influenzae* b, *Streptococcus pneumoniae*, *Neisseria meningitidis*, group B *Streptococcus*, and Listeria monocytogenes depending on age, sex, race, season and immunologic status of the child [2] [3] [4].

Acute bacterial meningitis is one of the deadliest and causes most disabling forms of this disease; it is epidemic-prone, can lead to death within 24 hours and leave one in five patients disabled for life as a result of an infection [3].

Several different bacteria can cause meningitis, but it is *Neisseria meningitidis* (Nm) that has the ability to cause large outbreaks [4]. Meningococcal meningitis is associated with a high fatality rate (up to 50% when untreated) and a high frequency of severe sequelae (over 10%). Until 2009, serogroups A and C were the most frequent in sub-Saharan Africa and the main causes of epidemics, serogroups W135 and X being of more recent emergence in this region.

The introduction and widespread distribution of MenAfriVac® (meningococcal A conjugate) vaccination since 2009 in subjects aged 1 to 29 have profoundly changed the epidemiology of meningitis [2].

After meningococcus, Streptococcus pneumoniae, a gram-positive diplococcus, is the second pathogen responsible for bacterial meningitis. It mainly affects

children under one year old, but can occur at any age, most often on risky sites (Eyes Noses and Throat infections, history of head trauma, alcoholism, splenectomy, sickle cell disease). Lethality, high in the tropics, can reach 50% [2].

Haemophilus influenzae, in countries that have not implemented Hib vaccination in infants, H. influenzae, a gram-negative bacillus, remains one of the major causes of meningitis in children under 5 years of age. H. influenzae meningitis is exceptional outside this age group. Mortality is again very high, around 50% [2].

Listeria monocytogenes, the typical picture is that of rhomb encephalitis with signs of brainstem involvement, in particular cranial nerve palsy.

In children under 2 months, the etiologies of meningitis are dominated by *Streptococcus agalactiae* (B), usually sensitive to ampicillin, and enterobacteria, sensitive to C3G [2].

The incidence of meningococcal disease increases with age; between 3 months and 1 year, pneumococcus is more common (nearly 50%), closely followed by meningococcus; after the age of 1 year, meningococcus and pneumococcus alone account for 95% of the causes of meningitis.

The main viral agents responsible (>70%) are enterovirus. Other viruses may be encountered: Epstein-Barr virus (EBV), cytomegalovirus, varicella-zona virus [1].

In the general population the attack rate of the 1-year and meningitis seems to affect infants under 3 months with predilection [1].

Worldwide, the annual number of cases is estimated at more than one million. Bacterial meningitis is the cause of high mortality in developing countries. In France, their overall incidence is 2.2/100,000 all ages combined. However, it is very high in infants (44/100,000), then decreases gradually (6.9/100,000 between 1 and 4 years [1].

The main pathogens responsible for viral meningitis vary by geographical region, season, and detection methodology. [5] In England and Wales, the most common causative agents of viral meningitis were enteroviruses (EVs), herpes simplex virus (HSV) and varicella zoster virus (VZV). In America, Leber, *et al.* reported that the most common causative agents of VE and VM were enteroviruses and human herpesvirus [6]. In Australia, the most common causative agents were HSV and VZV, while Japanese encephalitis virus was the most common causative agent of VE among children in southern Vietnam [5].

Meningitis is more acute in the African Meningitis belt, since 2010, member states in the meningitis have recorded an annual average of 24,000 suspected cases, resulting in 1800 deaths. The facility rate fluctuates between 5% and 14%, while 90% of cases are recorded during the epidemic season [7]. Since the Democratic Republic of Congo is also a member of these countries, it is not spared from cases of meningitis.

In the Eastern part of DRC, the carriage of pathogen in healthy children by real-time PCR, performed directly on the nasopharyngeal sample, pneumococci could be detected in almost all children (96%), whereas H. influenzae was de-

tected in 54% and B. pertussis in 10% [8]. Moreover, In DR Congo the antibiotic treatments available are entirely empiric due to insufficient microbiological diagnostics and, to our knowledge no studies exist which have assessed pathogens in the CSF of children hospitalized due to meningitis using multiplex real-time PCR assay.

Distinguishing children with bacterial meningitis from those with viral meningitis in the emergency department is sometimes difficult. This is why most authors recommend initiating antibiotic therapy in any child with acute meningitis at the slightest doubt, until the result of bacterial cultures of the cerebrospinal fluid (CSF) observed in 48 to 72 hours [4] [9].

The objective of our research was to determine the occurrence of bacteria and viruses in the CSF of hospitalised children with meningitis in the Eastern DR Congo. We also aimed to relate these findings to the outcomes. This is very important in our health community because it will help paediatricians to have an overview on the common local germ as it not possible to have RT/PCR test for children with clinical meningitis as the test is expensive however, the introduction of molecular techniques, such as multiplex real-time PCR, has the potential to improve diagnosis and patient outcomes as it gives precision on etiology.

2. Methods

2.1. Study Design

A cross-sectional and descriptive study with prospective data collected from the 1st of April 2021 to the 31st of March, 2022. The study was conducted to determine pathogens in the CSF of children hospitalized for meningitis at Panzi Hospital in the province of South Kivu in the Democratic Republic of Congo.

2.2. Study Site and Patients

The study was performed on hospitalized patients in the Pediatric department of Panzi Hospital. Panzi Hospital, located in Bukavu town, is a teaching hospital that served a population of 453,000 inhabitants including 86,000 (19%) children below 5 years at the time of the study [10] [11].

In our study, 251 children aged from 1 to 59 months old admitted for suspected meningitis to the pediatric department of Panzi Hospital, during our study period, *i.e.* from April 1, 2021 to March 31, 2022. A child was consider as clinic meningitis since he had fever associated to 2 or more than 2 of this symptoms: altered mental status, nausea, vomiting, sensitivity to light, headache, chills, stiff neck, bulging fontanel, purple areas of skin that resemble bruises, sleepiness, high-pitched crying, inconsolable behaviors, sleepy and difficulty waking, irritable and grumpy, doesn't feel well and has a weak suck during breastfeeding. He also must be negative for malaria test, HIV test and no history of head trauma but with an abnormal CSF (more than 10 white cells count and at list positive for protein of the CSF). The parent or guardian should sign the writing consent form to participate in the study. We also did a white cells count

and C-reactive protein for all cases.

From the 251 collected CSF samples and stored at −20˚C, only 150 were chosen randomly because of financial limitation and sent to the lancet laboratory in Kigali/Rwanda for a meningitis multiplex real-time PCR assay detecting the most relevant bacteria and virus causing meningitis. The characteristics of the 150 patients from whom the CSF was tested for bacteria identification are listed in the Table 1 (Table 1).

From the framework of routine medical practice, which includes medical history, clinical diagnosis and results, the following sociodemographic data were collected; gender, age in months, place of origin (urban or rural), vaccination status (considered complete when the child has already received 3 doses of pentavalent and 3 doses of pneumococcal conjugate vaccine 13 (PCV 13). The following clinical data were also collected; seizures, state of consciousness (defined by the AVPU scale: awake, verbal, pain, unresponsive), date of admission, date of discharge, history of antibiotic intake, referral or not, associated diseases and the nutritional status. The outcome was defined as death or cured.

Table 1. Characteristics of the children hospitalized due to meningitis at Panzi Hospital, Bukavu, DR Congo between April 1, 2021 and March 31, 2022 ($n = 150$).

Variables	Variable	Effective n (%)
Sex	Male	89 (59.3)
	Female	61 (40.7)
Age	<3 months	54 (36)
	3 - 24 months	40 (26.7)
	25 - 60 months	56 (37.3)
Vaccination	CV Complete	74 (49.3)
	Not vaccinated	76 (50.6)
Evolution	Death	45 (30.0)
	Improved	105 (70.0)
Saison	Rainy	94 (62.7)
	Dry	56 (37.3)
Address	Urban	94 (62.7)
	Rural	56 (37.3)
ATB used	Yes	73 (48.7)
	No	77 (51.3)
Refered	Yes	55 (36.7)
	No	95 (63.3)
Nutritional status	Not malnourished	124 (82.6)
	Malnourished	26 (17.3)

2.3. CSF Specimen Collection Followed by Bacterial and Viral Nucleic Acid Detection

In the pediatric unit, two samples, one milliliter (ml) of CSF were collected from each child who was suspected of having meningitis and were then immediately transported to the bacteriology laboratory of the Evangelical University in Africa. Then, approximately 0.5 ml of CSF was collected in a cryotube using a sterile serological pipette and stored at −20˚C for real-time PCR. The following tests were performed on the remaining 0.5 ml: macroscopic aspect and microscopic examination to determine, white cells count, and protein detection. After these analyses, the CSF samples that were stored in cryotubes at −20˚C for PCR were transported adequately through cold chain to the Lancet Laboratory in KIGALI/Rwanda. The Lancet laboratory has process a multiplex real-time PCR detecting the most frequent bacteria and virus causing meningitis using the allplex Meningitis Panel Assays according to Seneegee. This method target specific DNA sequence in a heterogeneous group of DNA sequences. The DNA sequence will be exponentially amplified through three major repeated steps. In the first step, double-stranded DNA will be denatured into a single-strand. In the second step, the sequence of the target complementary single strand will be shaped into a ring. In the third step, under the effect of thermostable DNA polymerase, the DNA sequences will be extended unidirectionally from 5' to 3' to produce double-stranded DNA molecules. The DNA molecule will be replicated and amplified at each step of extension, thus generating millions of copies of the original DNA molecule. Each copy was identified through fluorescent dyes. Real-time PCR combines amplification and detection into one step using fluorescent dyes.

2.4. Data Management and Statistical Analysis

Descriptive analysis was performed using the XLSTAT 2022 package (version 24.0) for the description of founded results**.** The detected bacteria and viruses in cases were compared to medical conditions or outcome by Pearson's chi-square or Fisher's exact test (if $n < 5$). Potential variables associated with differences between fatal and improving cases were assessed by odds ratios (OR) with 95% CI and were tested by univariable analysis with the Pearson's chi-square or Fisher's exact test (if $n < 5$). A p-value of <0.05 was considered statistically significant.

2.5. Ethics and Consent

The study was conducted in accordance with good clinical practice and good pharmacology and epidemiology practices. The study was approved by the National Health Ethics Committee of DR Congo (CNES/DP-SK 001-4125/001-155-2021). Written or witnessed and thumb written informed consent was obtained from the parent/legal representative of each study participant prior to enrolment.

2.6. Funding

This study was supported by the children prize foundation. The funding body had no role in the design of the study, the collection, analysis or interpretation of data, nor in the writing of the manuscript.

3. Results

Characteristics of the 150 children hospitalized due to meningitis and from whom the CSF has been tested by Real-Time PCR for bacteria identification are listed in the Table 1 (Table 1).

By Real-Time PCR we identify germs in 37/150 (24.7%) of cases (Table 2). We isolated bacteria in 25/37 (67.5%), viruses in 9/37 (24.3%) and virus and bacteria co-infection in 3/37 (8.1%) (Table 2). The most frequent bacteria were *Streptococcus Pneumoniae* 14/37 (37.8%) followed by *Haemophilus influenzae* 6/37 (16.2%) and *Streptococcus agalactiae* 5/37 (13.5%) among yang children, while the main virus was cytomegalovirus 5/37 (13.5%) (Table 2).

For *Streptococcus pneumonia*, 85.7% were more common in children aged between 25 - 60 months, and in 64.3% of children from rural areas. *Streptococcus pneumonia* was significantly higher among unvaccinated children (85.7%). (OR 4.00; 95% CI 1.06 - 14.99, p = 0.039) (Table 3). *Haemophilus influenzae* were more common in children between 3 - 24 months and in children from rural areas but this different was not significantly higher (Table 4). Cytomegalovirus was common in children aged 25 - 60 months (80.0%), most of them were from urban area (100%), and 80% among them have completed the scheduled vaccination program (Table 3 and Table 4).

Bacterial and virus co-infection were identified in 66.7% of children aged between 25 - 60 months, mainly among male children, and in 100% of children from urban areas (Table 4).

Streptococcus pneumoniae was more frequent in children who's C-reactive protein was higher and in those with high number of white blood cells in CSF. But virus was more found in samples with clear CSF (Table 2).

The overall case fatality rate was higher (30%) and was highest for co-infection CMV-Pneumococcal 66.7%, followed by those with *Streptococcus pneumoniae* (50%) (Table 5).

4. Discussion

Our results revealed that *Streptococcus pneumoniae* (*n* = 14) followed by *Haemophilus influenzae* (*n* = 6) were the most prevalent bacteria detected in the CSF of ours under five years children hospitalized for meningitis, similar results has been reported in Namibia in 2013 [12], in Mozambique [13], in Kenya at Kenyatta Hospital where streptococcus pneumonia was about 51.2% [14]. A study done in Manhiça, a rural area in Southern Mozambique has reported *Streptotoccus pneumoniae* (*n* = 31) as the most prevalent bacteria in the CSF of children with meningitis followed by, *Haemophilus influenzae* (*n* = 13) and

Neisseria meningitis (n = 8) [15]. But a study done in the pediatric department of the Hospital from Mali found that the main germs isolated were *Streptococcus pneumoniæ* (36.4%) followed by Neisseria *meningitidis* (12.5%) and then *Haemophilus influenzae* (9.1%) [16], while in our result we didn't isolate *Neisseria meningitidis*. This appearance of *Neisseria meningitides* as the second most prevalent bacteria in Malian study group, can be explains by the epidemic aspect of *Neisseria meningitides* [16].

Table 2. Laboratory results of the children hospitalized due to meningitis at Panzi hospital, Bukavu, DR Congo between April 1, 2021 and March 31, 2022 (n = 150).

Variables	Variable	Effective n (%)		
CRP	Neg	25 (16.7)		
	15 - 100	104 (69.3)		
	>100	21 (14)		
Aspect CSF	Cloudy	55 (36.7)		
	Clair	95 (65.3)		
Pleocytose	<10	90 (60)		
	10 - 99	23 (15.3)		
	≥100	37 (24.7)		
Hospitalisation duration	1 à 3 days	37 (24.7)		
	4 à 10 days	60 (40)		
	11 à 20 days	37 (24.7)		
	≥21 days	16 (10.6)		
Identified pathogens	Bacteria	25 (16.7)		
	Virus	9 (6)		
	Coinfection virus-bacteria	3 (2)		
	Aseptic	113 (75.3)		
			CRP ≥ 20 mg/dl	**GB ≥ 10,000**
RT/PCR of CSF	*Haemophilus Influenzae* (n = *6*)	14 (9.3)	6 (100)	6 (100)
	Streptococcus Pneumoniae (n = *14*)	6 (4)	14 (100)	14 (100)
	Streptococcus agalactiae (n = *5*)	5 (3.3)	5 (100)	5 (100)
	CMV (n = *5*)	5 (3.3)	4 (80)	5 (100)
	Herpes Virus (n = *4*)	4 (2.7)	3 (75)	3 (75)
	CMV+ *Pneumococcus pneumoniae* (n = *3*)	3 (2)	3 (100)	3 (100)
	Aseptic (n = 113)	113 (75.3)	81 (71.7)	89 (78.8)

Table 3. Microbiological findings among completed vaccinated children compared to uncompleted vaccinated children hospitalized due to meningitis at Panzi Hospital, Bukavu, DR Congo between April 1, 2021 and March 31, 2022 (n = 150).

Immunization	Vaccinated 74 (49.3)	Not vaccinated 76 (50.6)	OR (95% CI)	p-value
***Haemophilus influenzae* (n = 6)**	1 (16.5)	5 (83.3)	5.14 (0.58 - 45.10)	0.13
***Streptococcus pneumoniae* (n = 14)**	**3 (21.4)**	**11 (78.6)**	**4.00 (1.06 - 14.99)**	**0.039**
***Streptococcus agalactiae* (n = 5)**	0 (0)	5 (100)	11.46 (0.62 - 211.07)	0.100
CMV (n = 5)	4 (80)	1 (20)	0.23 (0.025 - 2.138)	0.197
Herpes virus (n = 4)	1 (25)	3 (75)	3.00 (0.304 - 29.516)	0.3463
CMV+ *Pneumococcus pneumoniae* (n = 3)	2 (66.7)	1 (33.3)	0.48 (0.042 - 5.409)	0.5526
Aseptic (n = 113)	51 (45.1)	62 (54.9)	1.99 (0.933 - 4.273)	0.074

Table 4. Microbiological findings by age groups among children hospitalized due to meningitis at Panzi Hospital, Bukavu, DR Congo between April 1, 2021 and March 31, 2022 (n = 150).

Variable n (%)	<3 months 54 (36)	3 - 24 months 40 (26.7)	25 - 60 months 56 (37.3)	From Urban	From Rural
***Haemophilus Influenzae* (n = 6)**	0 (0)	4 (66.7)	2 (33.3)	2 (33.3)	4 (66.6)
***Streptococcus Pneumoniae* (n = 14)**	0 (0)	2 (14.3)	12 (85.7)	13 (92.9)	1 (7.1)
***Streptococcus agalactiae* (n = 5)**	5 (100)	0 (0)	0 (0)	4 (80.0)	1 (20.0)
CMV (n = 5)	0 (0)	1 (20)	4 (80)	5 (100)	0 (00.0)
Herpes Virus (n = 4)	1 (25)	2 (50)	1 (24)	3 (75.0)	1 (25.0)
CMV+ *Pneumococcus pneumoniae* (n = 3)	0 (0)	1 (33.3)	2 (66.7)	3 (100)	0 (00)
Aseptique	48 (42.5)	30 (26.5)	35 (31)	113 (75.3)	98 (86.7)

Table 5. Microbiological findings among children hospitalized due to meningitis outcome and comparison between detected bacterial fatality to those with *Haemophilus influenzae*'s outcome (n = 150).

Variable (n)	Death 45 (30)	Improved 105 (70)	OR (95% CI)	p-value
***Haemophilus influenzae* (n = 6)**	2 (33.3)	4 (66.7)	1	
***Streptococcus pneumoniae* (n = 14)**	7 (50)	7 (50)	2.00 (0.272 - 14.699)	0.495
***Streptococcus agalactiae* (n = 5)**	2 (40)	3 (60)	1.333 (15.7047)	0.81
CMV (n = 5)	0 (0)	5 (100)	0.163 (0.006 - 4.357)	0.2797
Herpes virus (n = 4)	2 (50)	2 (50)	2.00 (0.149 - 26.73)	0.600
CMV+ *Pneumococcus pneumoniae* (n = 3)	2 (66.7)	1 (33.3)	4.00 (0.211 - 75.66)	0.355
Aseptic (113)	30 (26.5)	83 (73.5)	0.72 (0.125 - 4.151)	0.7160

More over the prevalence of *Streptococcus pneumoniae* and *Haemophilus influenzae* in our study groups, can be lead to the fact that there were several number included patient whose immunization against *Streptococcus pneumoniæ* and *Haemophylus influenzae* were not completed. Indeed, the benefits of the Hib vaccine and PCV13 on the onset the meningitis are well documented. [17] [18] [19] *Streptococcus pneumoniae*, a gram-positive diplococcus, is the second pathogen responsible for bacterial meningitis. It mainly affects children under one year old, but can occur at any age, most often on risky sites (eyes noses and throat infections, history of head trauma, alcoholism, splenectomy, sickle cell disease). Lethality, high in the tropics, can reach 50% [2].

In our result, we finds viruses in 9/37 (24.3%), that looks lower compared to other studies: A study done in Marrakech which showed viral meningitis in 52% of cases without specification [20]. In China, they found 42.8% of cases identified viral meningitis [21]. A study done in Quatar has found lower prevalence is compered to our result (10.9% of cases) [22].

The mains viruses were cytomegalovirus 5/37 (13.5%). Herpes Simplex viruses 2 were also found with low incidence (2.7%). Cerebromeningeal herpetic infection is rare in children, the incidence being estimated at 1 to 2 per 1 million inhabitants per year [1].

Many studies highlight enterovirus as principal causes of viral meningitis as it was finds in China [21]. In Qatar, the main causative virus was enterovirus 968.7%) in children under 10 years old but HSV-2 was found with low frequency [22].

Cytomegalovirus was common in 80% of children aged 25 - 60 months and 33.3% among children from urban areas. More common among unvaccinated children (66.7%), a similar result has been reported by Leber and Coll for whom CMV is predominantly positive in pediatric age groups [6]. Several authors find CMV in viral meningitis of children with immunodeficiency or with congenital CMV. The finding of CMV by CSF PCR in the presence of bacterial meningitis has been reported and may represent a false-positive finding possibly related to latent virus in the WBC in an immunocompetent CMV-seropositive host [6] [23], since we don't have information on the immunocompromise statue of our study group on HIV, we cannot determine clinical implications of the CMV detected in our study group. Different from our result on bacteria and virus co-infection N. Sorek and Coll has reported confection of meningococcus-CMV instead of pneumococcus-CMV this can be explained by some epidemic aspect of meningococcus [24].

Regardless of the germ found in CSF, elevated white blood cell count and CRP that were more likely to be PCR bacterial positive than samples without these characteristics in our study group, similar results has been observed in many African countries as described by Mignon du Plessis and Coll [25].

In Our results the overall case fatality rate was higher (30%) and was highest for co-infection CMV-Pneumococcal co-infection 66.7%, followed by those with *Streptococcus pneumoniae* (50%), similar to those finds in the Sourthen Mo-

zambique where the overall case fatality rate was 36%, and was highest for *H. influenzae* and pneumococcal meningitis (55% and 45%) [15]. In Madagascar, Rafaravavy found a high fatality rate of 42.6% [19].

The mortality rate for bacterial meningitis in children of all ages is 6.6%. It is heavier in young infants (11.6% before 2 months). It varies according to the germs, being the highest with group B streptococcus (9.6%), then pneumococcus (9.3%), and *Escherichia coli* (8.9%). It is lower with *Haemophilus influenzae* (4%) and with meningococci, all serogroups combined (2.7%) [1].

The prognosis of viral meningitis is linked to the precocity of treatment but remains very reserved in infants. Mortality is low [1].

5. Conclusion

Meningitis remains frequent among children aged from one to 59 months in Bukavu. Infants mostly when there are not vaccinated against pneumococcus. However, we noticed that, fatality rate increased when there is co-infection with bacteria and viruses that might need a higher attention, as this could lead to fatal outcomes.

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Conflicts of Interest

The authors declare no competing interests.

Authors' Contributions

AMB designed and supervised the study. JM, KM and MM collected data from all medical records of admitted patients. JTM and JY analyzed the data in close communication with AMB. JTM was mainly responsible for writing the manuscript, which was critically revised by AMB. All authors read and approved the final manuscript.

References

[1] Bourillon, A., Benoist, G., Chabrol, B., Cheron, G. and Grimprel, E. (2020) Pédiatrie pour le praticien. 7th Edition, Elsevier, Amsterdam.

[2] Awulachew, E., Diriba, K. and Awoke, N. (2020) Bacterial Isolates from CSF Sample and Their Antimicrobial Resistance Patters in among under-Five Children Sus-

pected for Meningitis in Dilla University Referral Hospital. *Infection and Drug Resistance*, **13**, 4193-4202. https://doi.org/10.2147/IDR.S264692

[3] World Health Organization (2021) Defeating Meningitis by 2030: A Global Road Map. World Health Organization, Genève. https://apps.who.int/iris/handle/10665/342010

[4] Brouwer, M.C., Tunkel, A.R. and Van De Beek, D. (2010) Epidemiology, Diagnosis, and Antimicrobial Treatment of Acute Bacterial Meningitis. *Clinical Microbiology Reviews*, **23**, 467-492. https://doi.org/10.1128/CMR.00070-09

[5] Chen, X., Guo, J., Li, J., Li, Q., Ai, J., Sun, S., *et al.* (2018) Serotypes of Human Enteroviruses Causing Pediatric Viral Encephalitis and Meningitis in Hebei Province, China, From 2013 to 2015. *Pediatric Investigation*, **2**, 98-104. https://doi.org/10.1002/ped4.12037

[6] Leber, A.L., Everhart, K., Balada-Llasat, J.-M., Cullison, J., Daly, J., Holt, S., *et al.* (2016) Multicenter Evaluation of BioFire FilmArray Meningitis/Encephalitis Panel for Detection of Bacteria, Viruses, and Yeast in Cerebrospinal Fluid Specimens. *Journal of Clinical Microbiology*, **54**, 2251-2261. https://doi.org/10.1128/JCM.00730-16

[7] Organisation mondiale de la Sante (2021) Cadre pour la mise en oeuvre de la strategie pour vaincre la meningite d'ici2030 dans la region africaine de l'OMS: Rapport du Secrétariat. Organisation mondiale de la Santé. Bureau régional de l'Afrique. https://apps.who.int/iris/handle/10665/346629

[8] Birindwa, A.M., Kasereka, J.K., Gonzales-Siles, L.G., Geravandi, S., Mwilo, M., Tudiakwile, L.K., *et al.* (2021) Bacteria and Viruses in the Upper Respiratory Tract of Congolese Children with Radiologically Confirmed Pneumonia. *BMC Infectious Diseases*, **21**, Article No. 837. https://doi.org/10.1186/s12879-021-06570-1

[9] Dubos, F., Moulin, F., Raymond, J., Gendrel, D., Bréart, G. and Chalumeau, M. (2007) Distinction between Bacterial and Aseptic Meningitis in Children: Refinement of a Clinical Decision Rule. *Archives de Pédiatrie*, **14**, 434-438. https://doi.org/10.1016/j.arcped.2006.12.009

[10] Birindwa, M., Jeanniere, M., Andersson, R., Mindja, A. and Nordén, R. (2020) Decreased Number of Hospitalized Children with Severe Acute Lower Respiratory Infection After Introduction of the Pneumococcal Conjugate Vaccine in the Eastern Democratic Republic of the Congo. *Pan African Medical Journal*, **37**, Article 211. https://doi.org/10.11604/pamj.2020.37.211.22589

[11] Organisation mondiale de la Sante (2014) Deuxième enquête démographique et de santé (eds-rdc ii 2013-2014). https://reliefweb.int/report/democratic-republic-congo/deuxi-me-enqu-te-d-mographique-et-de-sant-eds-rdc-ii-2013-2014

[12] Mengistu, A., Gaeseb, J., Uaaka, G., Ndjavera, C., Kambyambya, K., Indongo, L., *et al.* (2013) Antimicrobial Sensitivity Patterns of Cerebrospinal Fluid (CSF) Isolates in Namibia: Implications for Empirical Antibiotic Treatment of Meningitis. *Journal of Pharmaceutical Policy and Practice*, **6**, Article No. 4. https://doi.org/10.1186/2052-3211-6-4

[13] Haimbodi, E.L., Mukesi, M., Mtambo, O. and Moyo, S.R. (2016) Frequency of Bacterial Organisms Isolated from Cerebrospinal Fluid (CSF) of Children under Five Years in Windhoek from 2010 to 2014. *Open Journal of Medical Microbiology*, **6**, 125-132. https://doi.org/10.4236/ojmm.2016.63017

[14] Serem, J.J., Chege, M. and Maina, D. (2018) Predictors of Bacterial Meningitis among Paediatric Patients Aged 0-5 Years at Kenyatta Hospital., Kenya. *Open*

Journal of Pediatrics, **8**, 207-220. https://doi.org/10.4236/ojped.2018.83023

[15] Sigaúque, B., Roca, A., Sanz, S., Oliveiras, I., Martínez, M., Mandomandoab, I., *et al.* (2008) Acute Bacterial Meningitis among Children, in Manhiça, a Rural Area in Southern Mozambique. *Acta Tropica*, **105**, 21-27. https://doi.org/10.1016/j.actatropica.2007.01.006

[16] Kané, B., Abdou, M., Koné, O., Dembélé, G., Diallo, K.W., Fané, B., *et al.* (2020) Causes of Bacterial Meningitis in Children from 1 Month to 15 Years in the Department of Pediatrics at Hopital du Mali from 2012 to 2018. *Revue Malienne d'Infectiologie et de Microbiologie*, **15**, 72-76. https://doi.org/10.53597/remim.v15i2.1736

[17] Haddad-boubaker, S., Lakhal, M., Fathallah, C., Bouafsoun, A. and Kharrat, M. (2018) Molecular Diagnosis of Bacterial Meningitis by Multiplex Real Time PCR in Tunisian Children. *The Journal of Infection in Developing Countries*, **12**, 235-243. https://doi.org/10.3855/jidc.9650

[18] Scott, S., Altanseseg, D., Sodbayer, D., Nymadawa, P., Bulgan, D., Mendsaikhan, J., *et al.* (2013) Impact of *Haemophilus influenzae* Type b Conjugate Vaccine in Mongolia: Prospective Population-Based Surveillance, 2002-2010. *The Journal of Pediatrics*, **163**, S8-S11. https://doi.org/10.1016/j.jpeds.2013.03.024

[19] Rafaravavy, N.E., Randrianjafinimpanana, H. and Robinson, A.L. (2014) SFP P-092—Profil bactériologique de la méningite de l'enfant hospitalisé à Tsaralalana Madagascar. *Archives de Pediatrie*, **21**, 802. https://doi.org/10.1016/S0929-693X(14)72062-7

[20] El Fakiri, K., Bourrous, M., Diffo, C., Rada, N., Draiss, G. and Bouskraoui, M. (2016) Les méningites du nourrisson et de l'enfant au centre hospitalier universitaire de Marrakech: Expérience d'une unité pédiatrique marocaine. *Journal de Pediatrie et de Puericulture*, **29**, 237-243. https://doi.org/10.1016/j.jpp.2016.08.002

[21] Ai, J., Xie, Z., Liu, G., Chen, Z., Yang, Y., Li, Y., *et al.* (2017) Etiology and Prognosis of Acute Viral Encephalitis and Meningitis in Chinese Children: A Multicentre Prospective Study. *BMC Infectious Diseases*, **17**, Article No. 494. https://doi.org/10.1186/s12879-017-2572-9

[22] Mathew, S., Al Khatib, H.A., Al Ansari, K., Nader, J., Nasrallah, G.K., Younes, N.N., *et al.* (2021) Epidemiology Profile of Viral Meningitis Infections among Patients in Qatar (2015-2018). *Frontiers in Medicine*, **8**, Article 663694. https://doi.org/10.3389/fmed.2021.663694

[23] Vicetti Miguel, C.P., Mejias, A., Ramilo, O., Ardura, M.I. and Sánchez, P.J. (2016) Cytomegalovirus Meningitis in an Infant with Severe Combined Immunodeficiency. *Journal of Pediatrics*, **173**, 235-237. https://doi.org/10.1016/j.jpeds.2016.02.054

[24] Sorek, N., Ashkenazi, S., Livni, G. and Ben-Zvi, H. (2019) *Neisseria meningitidis* and Cytomegalovirus Simultaneous Detection in the Filmarray Meningitis/Encephalitis Panel and Its Clinical Relevance. *IDCases*, **17**, e00516. https://doi.org/10.1016/j.idcr.2019.e00516

[25] du Plessis, M., de Gouveia, L., Freitas, C., Abera, N.A., Lula, B.S., Raboba, J.L., *et al.* (2021) The Role of Molecular Testing in Pediatric Meningitis Surveillance in Southern and East African Countries, 2008-2017. *The Journal of Infectious Diseases*, **224**, S194-S203. https://doi.org/10.1093/infdis/jiab092