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### ACTUALITIES IN PEDIATRIC MENINGITIS AFTER A DECADE OF EXPERIENCE

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#### Background

Pediatric meningitis is a serious illness resulting from meninges inflammation which can be caused by bacteria, viruses or other infectious and non-infectious agents. A crucial role in severity of the infection plays bacterial meningitis. It is associated with high morbidity and mortality. Survivors commonly develop neurologic sequelae.

Therefore, meticulous attention must be paid to prompt recognition, timely treatment, and close monitoring of children with this disease. Every pediatrician has to be alert to classical signs and symptoms (Fever, Headache, Meningeal signs (Kernig and Brudzinski) in order not to lose not a single case from an early and prompt diagnosis.

In neonates and infants' signs are less specific such as: poor feeding, lethargy, irritability, inconsolability and increased crying when being held, fever or hypothermia, seizures, bulging fontanelle, jaundice etc.

Considering the importance of the infection and the impact that it has in children health, we analyzed the children with meningitis hospitalized in our hospital which is the only tertial medical center of Albania. The demographic data of 2022 reveals a population of 2 829 109 inhabitants, 374800 of which live in urban area of Tirana city, Pediatric age (0-14 years) accounts for 16,3% of total population (1).

Vaccines against H. Influenzae and Str. Pneumoniae (PCV13), MMR are included at the mandatory national schedule of immunization, offered free of charge for all children.

Aim of this study is to analyze epidemiological and etiological data of acute Meningitis of pediatric age, admitted to Pediatric infectious diseases Service of University Hospital Center Mother Teresa during last decade, to evaluate natural trend of this infection and factors that influenced in their natural course.

To find out the impact of pandemia of Covid 19 (if any) in the prevalence of this important invasive infection.

## Material and Methods

Study design and location: This 10 year (2014 – 2023) retrospective cohort study included all the children aged 1month – 14 years, admitted to UNHMT diagnosed as Meningitis. The diagnosis was established on.

Bacteria isolated from the CSF obtained via LP, CSF bacterial culture, CSF molecular assays (polymerase chain reaction [PCR] or other nucleic acid amplification tests (NAAT)). Meningeal inflammation demonstrated by increased pleocytosis, elevated protein level, and low glucose level in the CSF.

Bacterial meningitis score (2,3) is used, when bacteriological signs were not available.

Components of the bacterial meningitis score are as follows:

- Positive CSF Gram stain
- CSF absolute neutrophil count 1000/ $\mu$ L or higher
- CSF protein level 80 mg/dL or higher
- Peripheral blood absolute neutrophil count 10,000/ $\mu$ L or higher
- History of seizure before or at the time of presentation.

We reviewed the medical records, and obtained LCS data, analyzed by biochemical methods and microbiological studies. Epidemiological characteristics as age, gender, chronology of infections and incidence, were analyzed. Etiological data were provided by Central Laboratory of UHCMT and national laboratory of microbiology and investigations in National Institute of Public Health in Tirana.

The diagnosis of viral meningitis was based on: negative LCS culture, slight pleocytosis with normal protein, normal glucose values, confirmation of the virus by PCR, serology, or underlying viral disease (varicella, measles etc.).

Data are analyzed by SPSS and X2 and Meen Whitney test were applied.  $P < 0.05$  was considered significant.

## Results

186 children with meningitis were identified. 105 cases were with bacterial meningitis, 54 with viral and a small group of 33 patients (with negative microbiology and ambiguous LCs data) were with unconfirmed etiology.) Male (107- 57.5%) dominate among infected children as usual in infections, although in some etiological agent we found females significantly more affected ( $p < 0.04$ ).

The age distribution was as follows: 37 patients (19,8%) were younger than 12 months of age, 43 patients (23.3%) were 1 – 4 years of age, 106 patients (56.9%) were 4 - 14 of age, with a significant predomination of cases above 4 years of age. Bacterial meningitis was the most common etiological factor for children younger less than 4 years, while viral meningitis is found more above this age (fig 1).

The distribution of living area is divided into urban and rural areas where urban areas dominated with 176 cases (94.6%) and only 10 patients (4.4%) came from rural areas.

The majority of cases was recorded in Autumn with 56 patients (30,2%), followed by Summer with 44 patients (23,6%) and an equal number of cases in Winter and Spring with 43 patients (23,1%).

The incidence of meningitis by year are shown in (fig 2). As we see there was un significant decrease during the pandemic years with an increase of number of cases during 2023, more

than mean values or pre Covid 19 period ( $p < 0.02$ ). The mean incidence of bacterial meningitis during this decade was calculated 140/105 children for all bacterial causes.

The etiologic agents are shown in table 1.

As we see, the 3 main agents remain, *N. meningitidis*, *Str. Pneumoniae* and less *H. influenzae*, nevertheless a good coverage of immunization schedule. There were found even not common bugs as Group *Streptococcus* in 3 cases, usually associated with a primary infective focus, in our cases, respectively: sinusitis and mastoiditis. Our cases had a benign course without permanent sequelae. Usually, opportunistic microorganism are the main causes of bacterial meningitis in infants younger than 3 months.

Among viral agents causing meningitis, we found in more than 60 % enterovirus, followed by varicella zoster virus, Measles, herpes virus 6, West Nile virus and Sars Cov 2.

Important complications were found in 18% of children with bacterial meningitis, subdural empyema, brain abscess, hydrocephaly, persistence of seizures, some extra neurological complications as Purpura Schoenlein Henoch, Pericarditis, erythema nodosum. The most severe case was those associated with sepsis, multiorgan failure, severe hyponatremia, mainly caused by *N. meningitidis* and *Str. Pneumoniae*. And those with very young age, who developed different sequels. The overall case fatality rate was 1%.

### Discussion

Bacterial meningitis is an important invasive infection of pediatric age. It affects more younger children and infants and our data concord with that of literature where similar incidence is found in this age group. (4,5) Beyond the neonatal period, the 3 most common organisms that cause acute bacterial meningitis are *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophiles influenzae type b (Hib)* same found even in other studies in Europe and USA.

The routine use of pneumococcal vaccine has also resulted in a > 98 % decline of invasive disease and 80% of resistant *S pneumoniae meningitis* cases. The incidence of invasive *Haemophiles influenzae* disease has declined by > 99%. (6,7) Similarly, the rates of meningococcal meningitis have dramatically decreased since the 1990s. nevertheless, these 3 remain the most common causative agents of bacterial infection especially in younger children. The risk factors for meningitis seems to be: age less than 2 years, incomplete immunization, immunocompromising conditions, cranial structure defects. The decrease of incidence during Covid 19 pandemic seems to be related not only with the lock down, but some studies showed that *Sars Cov2* by itself decrease the incidence of invasive infections (8,9) the increase of the incidence after 2022 in our country seems to be related with some gaps in routine immunization, modification of ecosystem, changes in host immunity.

*Streptococcus group A meningitis* although an uncommon course for meningitis is reported by other authors in different papers, (10,11, 12), usually associated with another infective conditions such as otitis media, sinusitis, skull infection etc. (12) Despite their findings showed a very severe and complicate course, our cases had a total improvement.

The positivity of culture usually it's not as high as we can expect, up to 60-70% referred by other authors, because of previous treatment with antibiotics, negative gram smears, pleocytosis between 500-1000 cells, without significant values of proteinorrachia and glycorrachia. That why, today the researches are concentrated in other biochemic markers as procalcitonin, Interleukin 6, lactate concentration in CSF which can be significantly higher in BM. (13,14) Despite improvements in antibiotic and supportive therapy, death and complication rates remain significant. Mortality and morbidity depend on the infectious agent, the age of the child, the child's general health, and the promptness of diagnosis and treatment. This rate varies by

organism, with S pneumoniae being associated with the highest rate of complications. (15) These complications include, purulent intracranial complications, sepsis with multiorgan failure, and permanent sequelae as nerve deafness, cortical blindness, hemiparesis, quadriparesis, muscular hypertonia, ataxia, complex seizure disorders, mental motor retardation, learning disabilities, obstructive hydrocephalus, and cerebral atrophy.

The rigorously implementation of immunization schedule is always a very important issue in children health.

**Conclusions**

Bacterial meningitis still is an important invasive infection among young children nevertheless contentious improvement of immunization schedule and very good coverage 98% for Albanian children).

The determination of causative agent and their serotyping remain a challenge for our pediatricians

Cocid 19 pandemic has modified the natural course of meningitis in children like as in other infections.

The main focus rare 3 major causative agents N. Meningitides, str, pneumoniae and H. influenzae without neglected other etiological agents depending on age, predisposing factors and underlying diseases.

Age group	Bacterial pathogens
0-3 months	Streptococcus sp, E coli, Staphylococcus spp., S.marcescenes, Corinebacterium durum, Bacillus citreus,etc.
4 months-1 year	H. influenzae, N.meningitidis, Str. Pneumoniae, Staphylococcus spp.
1-4 years	N. meningitidis, Str. Pneumoniae, Staphylococcus sp.
4-14 years	Str. Pneumoniae, N. meningitidis, Str. Pyogenes

Table 1. The most common bacterial agents.

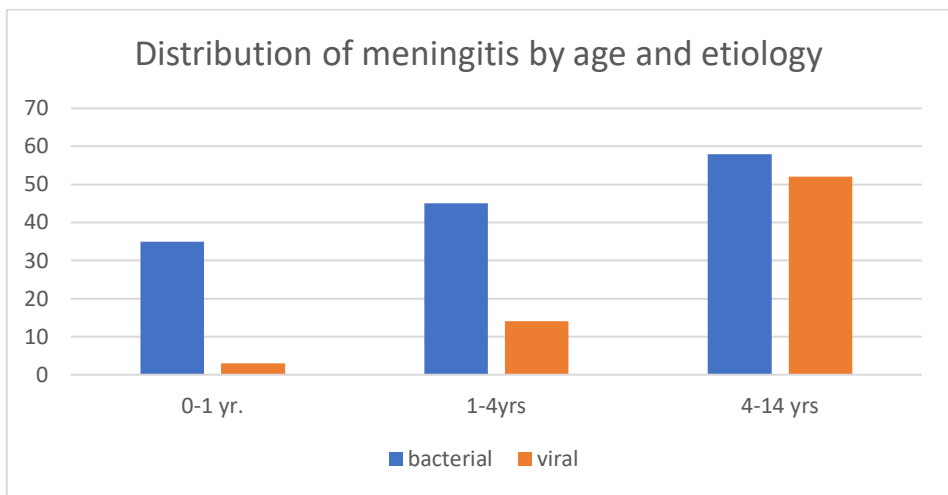


Fig. 1 Age distribution of meningitis.

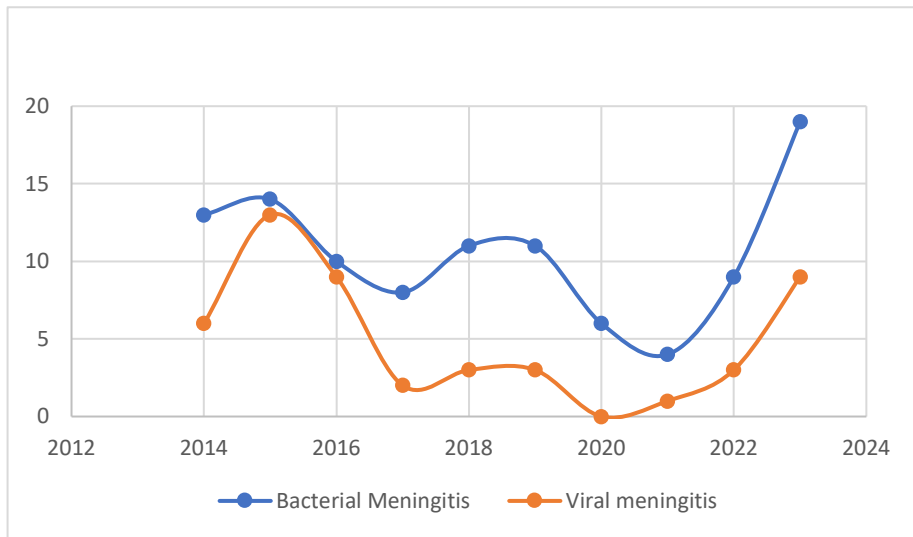


Fig. 2 Incidence of pediatric meningitis (2014-2023).

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