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**ORIGINAL ARTICLE**

# CHILDHOOD MENINGITIS IN AN URBAN TERTIARY MEDICAL CENTER: A 20-YEAR REVIEW

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The authors declare that the data presented are original material and has not been previously published, accepted or considered for publication elsewhere; that the manuscript has been approved by all authors, and all authors have met the requirements for authorship.

## ABSTRACT

**Background:** Meningitis is a neurological emergency causing significant morbidity and mortality. This research determined the etiologies, clinical presentation, and ancillary work-up findings of different types of meningitis.

**Objective:** To characterize the documented pediatric meningitis cases in a tertiary hospital admitted between January 1, 1997 to August 31, 2017.

**Methods:** This was a retrospective study which entailed review of charts of all pediatric cases 0 to 18 years old with a discharge diagnosis of meningitis (bacterial, viral, tuberculous or fungal) from January 1, 1997 to August 31, 2017 at an urban tertiary medical center.

**Results:** This study included 127 subjects, where 74 (58.3%) had bacterial, 34 (26.8%) had viral, 17 (13.4%) had tuberculous, and 2 (1.6%) had fungal meningitis. *Streptococcus pneumoniae* (12.2%), *Haemophilus influenzae* type b (6.8%) and *Salmonella enteritidis* (6.8%) were the top bacteria identified. Neonatal infections were caused by gram-negative bacilli (66.7%) and gram-positive cocci (33.3%). Bacterial, tuberculous, and viral meningitis were seen in the 1-11 months, 2-4 years and 5-10-year age groups respectively. Prolonged fever (mean 27.2, median 14 days) and cranial nerve palsies (23.5%) were noted in tuberculous meningitis (TBM). The highest CSF mean WBC (2043±9056 WBC/μL) and mean protein (300±365.6mg/dL) were seen in bacterial and tuberculous meningitis respectively. The combination of hydrocephalus, basal enhancement and infarct was unique to patients with tuberculous meningitis. Recurrent seizures were the most common complication of bacterial (36.5%), viral (20.6%) and tuberculous (100%) meningitis. Ceftriaxone (24.3%), acyclovir (38.2%), and isoniazid/rifampicin/pyrazinamide/ethambutol (76.5%) were the most common antimicrobials for bacterial, viral, and tuberculous meningitis. Fever duration before admission was significantly longer in TBM (14 days) than in viral (4 days) and bacterial meningitis (2 days). Length of hospital stay for viral meningitis (6.5 days) was significantly shorter than for TB (14 days) and bacterial meningitis (12 days). Mortality rates were 12% and 11% for bacterial and viral meningitis respectively. No mortality was seen in patients with TB and fungal meningitis.

**Conclusions:** In this 20-year review of childhood meningitis, bacterial meningitis was the most common type of pediatric meningitis which presented with marked CSF pleoctyosis. The longest fever duration and the highest proportion of cranial nerve involvement were seen in TBM, which also had the unique combined findings of leptomeningeal enhancement, hydrocephalus and infarct on imaging. Ceftriaxone was the most commonly used antibiotic for bacterial meningitis, except in neonates where a combination of cefuroxime-amikacin was initially given until microbiological confirmation became available. Recurrent seizures were the most common complication of bacterial, viral and TB meningitis. The shortest hospital stay with the highest full recovery rate was seen in viral meningitis.

**KEYWORDS**: *meningitis, clinical manifestations, ancillary findings, treatment, outcomes*

## INTRODUCTION

Meningitis is a life-threatening disease, and despite the availability of vaccines, effective antimicrobials and advances in critical care, it still belongs to the Department of Health's (DOH) top 10 causes of childhood mortality[1]. Based on the Philippine Pediatric Society (PPS) registry, meningitis of different etiologies accounts for only a small percentage of all reported illnesses (0.72%) in the past ten years. However, these infections have a significant mortality rate (9 to 19%)[2]. Meningitis is caused by different pathogens that produce similar symptomatology. This underscores the importance of seeking microbiological confirmation for definitive management. The high risk for significant pediatric morbidity and mortality that this disease confers calls for prompt management pending microbiologic confirmation.

The etiologies of meningitis are age- and setting-specific and may vary over time as a function of local vaccination policies and practices hence, epidemiologic data are indispensable. Locally, the most common bacterial pathogens in the different pediatric age groups are: gram negative enteric bacilli for neonates and infants up to 2 months of age and Hemophilus *influenzae type b* and *Streptococcus pneumoniae* for infants and children 3 months to less than 5 years old. *Neisseria meningitidis* may occur sporadically or in epidemics, with 80-90% of cases presenting as meningitis[3]. *Mycoplasma pneumoniae*, a common cause of respiratory tract infection in children 5 years and up, can also cause central nervous system complications. Meningitis and meningoencephalitis are its most common extra- pulmonary complications, affecting about 2.6 to 7% of patients with *Mycoplasma pneumoniae* infection[4]. Enteroviruses (i.e., coxsackievirus B, echoviruses) are the leading causes of viral meningitis in children, after the advent of mumps, measles, and rubella (MMR) vaccination. In addition, non-polio human enteroviruses are also a leading cause of aseptic meningitis (80-92%). Other common causes are herpes simplex virus (HSV) and varicella zoster virus (VZV)[5,6]. Tuberculous meningitis (TBM) is the most severe form of tuberculosis (TB). It is associated with a 16% mortality and 33% risk of intermediate or severe disability among survivors at the end of treatment, with the highest risk seen among infants and children under 2 years of age[7]. The likelihood of TBM increases in the presence of a sub-acute course, involvement of cranial nerves, and basal enhancement on CT scan[8,9,10]. Fungal meningitis is relatively rare. The most common cause of fungal meningitis is *Cryptococcus neoformans*, with an incidence of 0.016-100 cases/100,000 children. It should be considered in any child with fever, prolonged headache, vomiting and focal neurologic signs[11,12,13,14]. When used in conjunction with clinical and laboratory findings, epidemiologic data can guide the clinician in the diagnosis and in the choice of empiric antimicrobials.

In a resource-deficient country like the Philippines, reducing morbidity and mortality relies heavily on reliable local data on the clinical profile and epidemiology of CNS infections. Identification of age- and setting-specific etiologic agents is important to help the clinician in empiric treatment before results of diagnostic work-ups become available. This study was undertaken to characterize the documented pediatric meningitis cases in a tertiary hospital admitted between January 1, 1997 to August 31, 2017. Specifically, this study was done to (1.) determine the distribution of cases according to major etiologies of meningitis (bacterial, viral, tuberculous and fungal); (2.) to describe the age distribution, age distribution, clinical manifestations, ancillary work-up results, length of admission, treatment, complications and outcomes for each major etiologies; and (3.) to compare them as to their range and median duration of fever, range and median length of hospital stay and proportion of various outcomes.

## METHODOLOGY

### Study Design and Setting

This was a retrospective study where records of patients admitted between January 1, 1997 to August 31, 2017 with a discharge diagnosis of meningitis (bacterial, viral, tuberculous or fungal meningitis) were identified and reviewed.

### Method

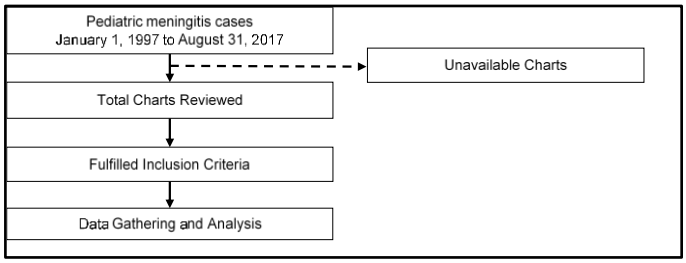


**Figure 1.** Flow of Study Participants

### Inclusion Criteria

All admitted pediatric patients who had a final diagnosis of meningitis (bacterial, viral, tuberculous or fungal) were included in the study.

### Exclusion Criterion

Patients diagnosed with meningitis, but who did not undergo CSF analysis, were excluded.

### Data Gathering

Demographic, clinical, and microbiological information for each patient were collected from the medical records. The patient list was obtained from the ArchiveOne database, census of floors and ICU admissions from previous years, and records of infectious disease specialists and neurologists. Data collection lasted for two months.

### Data Processing

Data encoding was done using Microsoft Excel, and completeness, consistency, and errors among the answers were checked.

### Statistical Analysis

Data analysis was performed using STATA version 15. Mean and standard deviation were used to present quantitative data. Frequency distributions were used for categorical data. Kruskal-Wallis Test was used to compare quantitative data by etiology, followed by Dunn's test as post-hoc test. Chi-square Test or Fischer's Exact Test, whichever was applicable, was used to compare categorical data. All p-values less than 0.05 were considered statistically significant.

### Ethical Considerations

The study was conducted according to the ethical principles based on the Declaration of Helsinki, WHO guidelines, and International Harmonization—Good Clinical Practice, and National Ethics Guidelines for Health Research. The research protocol underwent approval by the Institutional Review Board (IRB).

## RESULTS

### Demographic Data

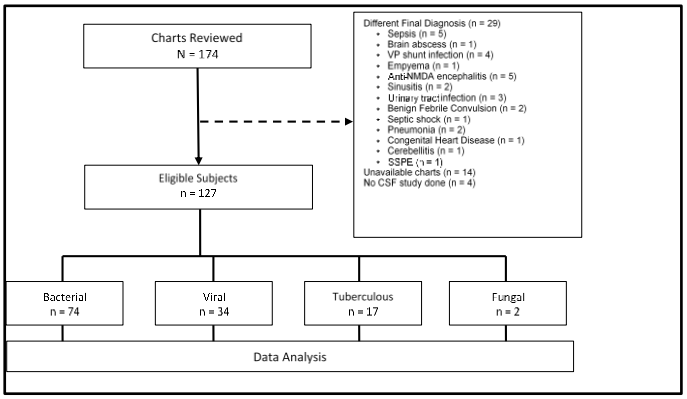


**Figure 2.** Methodology Flowchart

A total of 174 cases were identified based on the data gathering process stated earlier, but only 127 were included in the data analysis (see figure 2). Forty-seven cases were excluded, of which 29 did not have meningitis

as a final diagnosis upon rechecking of charts, 4 had no CSF studies, and 14 were unavailable.

Of the 127 patients, 74 (58.3%) had bacterial, 34 (26.8%) had viral, 17 (13.4%) had tuberculous and 2 (1.6%) had fungal meningitis. A male predilection was demonstrated for all except fungal meningitis.

Incidence peaked at two age groups: 1-11 months (25.2%) and 5-10 years old (23.6%). The most common age group for the different types of meningitis were: 1-11 months old for bacterial meningitis, 2-4 years old for TBM, and 5-10 years old for viral meningitis.

Bacterial Meningitis

**Table 1.** Specific Etiologic Agents and Age Group Distribution for Bacterial Meningitis, January 1, 1997 to August 31, 2017 (n=74)

| Etiologic agent | 0-7 days No.(%) | 8-30 days No.(%) | 1-11 months No.(%) | 12-23 months No.(%) | 2-4 years No.(%) | 5-10 years No. (%) | 11-15 years No.(%) | 16-18 years No.(%) | Total (%) |
|---|---|---|---|---|---|---|---|---|---|
| th Organisms Isolated | | | | | | | | | **41 (55.4)** |
| Gram Positive | | | | | | | | | **18 (24.3)** |
| *Streptococcus pneumoniae* | 0(0.0) | 0(0.0) | 4 (5.4) | 1 (1.4) | 2(2.7) | 2(2.7) | 0(0.0) | 0(0.0) | 9(12.2) |
| *CONS (Staphylococcus epidermidis, capitis, staphylococcus hemolyticus)* | 0(0.0) | 1 (1.4) | 3(4.1) | 0(0.0) | 0(0.0) | 0(0.0) | 1(1.4) | 0(0.0) | 5(6.8) |
| *Streptococcus agalactiae (GBS)* | 0 (0.0) | 2(2.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0(0.0) | 0 (0.0) | 0 (0.0) | 2(2.7) |
| *Micrococcus spp.* | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0(0.0) | 1 (1.4) | 0 (0.0) | 1(1.4) |
| *Oxacillin-Resistant Staphylococcus aureus*(ORSA) | 0 (0.0) | 1 (1.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0(0.0) | 0 (0.0) | 0 (0.0) | 1(1.4) |
| Gram Negative | | | | | | | | | **23 (31.1)** |
| *Hemophilus influenzae B* | 0 (0.0) | 0 (0.0) | 4 (5.4) | 1 (1.4) | 0 (0.0) | 0(0.0) | 0 (0.0) | 0 (0.0) | 5(6.8) |
| *Salmonella enteritidis* | 0 (0.0) | 1 (1.4) | 3 (4.1) | 0 (0.0) | 0 (0.0) | 0(0.0) | 0 (0.0) | 0 (0.0) | 4(5.4) |
| *Neisseria meningitides* | 0 (0.0) | 1 (1.4) | 2 (2.7) | 0 (0.0) | 0 (0.0) | 0(0.0) | 0 (0.0) | 0 (0.0) | 3(4.1) |
| *Elizabethkingia meningoseptica/ Flavibacterium Meningosepticum/ Chryseomonas meningospetica* | 2 (2.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (1.4) | 0(0.0) | 0 (0.0) | 0 (0.0) | 3(4.1) |
| *Acinetobacterspp* | 0 (0.0) | 1 (1.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0(0.0) | 0 (0.0) | 0 (0.0) | 1(1.4) |
| *Pseudomonas aeruginosa* | 0 (0.0) | 0 (0.0) | 1 (1.4) | 0 (0.0) | 0 (0.0) | 0(0.0) | 0 (0.0) | 0 (0.0) | 1(1.4) |
| *E. coli* | 0 (0.0) | 0 (0.0) | 1 (1.4) | 0 (0.0) | 0 (0.0) | 0(0.0) | 0 (0.0) | 0 (0.0) | 1(1.4) |
| *Klebsiella pneumonia* | 0 (0.0) | 0 (0.0) | 1 (1.4) | 0 (0.0) | 0 (0.0) | 0(0.0) | 0 (0.0) | 0 (0.0) | 1(1.4) |
| *Burkholderia cepacia* | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0(0.0) | 1 (1.4) | 0 (0.0) | 1(1.4) |
| *Proteus mirabilis* | 0 (0.0) | 1 (1.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0(0.0) | 0 (0.0) | 0 (0.0) | 1(1.4) |
| *Serratia marcenscens* | 0 (0.0) | 1 (1.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0(0.0) | 0 (0.0) | 0 (0.0) | 1(1.4) |
| *Enterobacter cloacae* | 0 (0.0) | 1 (1.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0(0.0) | 0 (0.0) | 0 (0.0) | 1(1.4) |
| organism isolated | 0 (0.0) | 3 (4.1) | 7 (9.5) | 0 (0.0) | 5 (6.8) | 13(17.6) | 4 (5.4) | 1 (1.4) | **33(44.6)** |

In bacterial meningitis, 55.4% of cases had organisms identified either by culture (CSF and/or blood), by latex agglutination or by CSF Gram's staining. Among these laboratory-confirmed cases, 31.1% were due to gram-negative organisms. Overall, the most commonly-isolated organism was *Streptococcus pneumoniae* (12.2%). The other commonly identified organisms were *Haemophilus influenzae* type b (Hib) (6.8%), coagulase-negative staphylococci (CONS) (6.8%) and *Salmonella enteritidis* (5.4%). See table 1.

*Streptococcus pneumoniae* was seen in children 1 month to 10 years old. All cases of Hib meningitis were in children younger than 2 years old, with 80% of cases seen below 12 months. Eighty percent of CONS cases were seen in those younger than 12 months, while the remaining 20% were seen in 11-15-year-old-adolescents. All *Salmonella enteritidis* cases were seen in children below 12 months old.

Among neonates, 66.7% of infections were due to gram-negative bacilli, while the remaining 33.3% were caused by gram-positive cocci such as Group B Streptococcus (GBS), oxacillin-resistant *Staphylococcus aureus* (ORSA), and coagulase-negative staphylococci (CONS). Both of the GBS cases (100%) were seen in neonates. Other than Hib, Salmonella, and meningococcus, four gram-negative bacilli (*Acinetobacter* spp., *Proteus mirabilis, Serratia marcescens and Enterobacter cloacae*) caused late-onset neonatal sepsis/meningitis, while three other gram-negative organisms (*Pseudomonas aeruginosa, E. coli, and Klebsiella pneumoniae*) were seen among infants between 1-11 months. All three (100%) meningococcal cases were seen in infants less than 1 year of age.

There were eleven (14.9%) presumed *Mycoplasma pneumoniae* infections, based on a positive serum Mycoplasma IgM result. The majority (54.5%) were seen in the 5-10-year-old age group.

The most common clinical manifestation of bacterial meningitis was fever (81.1%), with a mean duration of 5.7±12.2 days. Majority (64%) of afebrile cases were in neonates, whose most common manifestations were respiratory distress (40%), seizures (26.7%), bulging fontanel (26.7%) and poor feeding (20%). Across all ages, the more commonly seen clinical manifestations were seizures (48.7%),

vomiting (29.7%), neck stiffness (23%) and bulging fontanel (20.3%). Cranial nerve palsies were observed in 10.8% of cases, with cranial nerves IV, VI and VII being more frequently affected. Of the 11 presumed *Mycoplasma pneumoniae* meningitis cases, 4 (36.4%) had respiratory symptoms such as cough (27.3%) or cough with colds (9.1%) on admission.

**Table 2.** Summary of CSF and Blood Test Results for Bacterial, Viral, Tuberculous and Fungal Meningitis Cases admitted from January 1, 1997 to August 31, 2017 (n=127)

| | Bacterial Meningitis (n=74) | Viral Meningitis (n=34) | Tuberculous Meningitis (n=27) | Fungal Meningitis (n=2) |
|---|---|---|---|---|
| **CSF** | | | | |
| WBC count (WBC/µL) | 2043±9057 (range: 1-12,240) | 50.9±179.6 (range 1-945) | 163.8±180.2 (range: 0-651) | 77±17 |
| Lymphocytes (%) | 36.2±34.3 | 39±37.1 | 65.2±38.9 | 73±17 |
| Neutrophils (%) | 46±37.5 | 19.3±24.3 | 11.8±16.4 | 4±4 |
| Protein (mg/dL) | 248.6±405.1 | 77.6±73.9 | 300±365.6 | 63.9±4.9 |
| Glucose (mg/dL) | 40.7±64.9 | 66.1±20.3 | 47.2±29.1 | 4.5±0.5 |
| **Blood** | | | | |
| WBC ($x10^3$/µL) | 16.8±10.2 | 11.5±5.4 | 11±3.2 | 5.8±0.8 |
| Lymphocyte (%) | 27.4±17.7 | 44.6±29.4 | 25.8±16.9 | 20±16 |
| Neutrophil (%) | 62.3±20.1 | 50.3±27 | 64.2±19.4 | 58±6 |

For all cases of bacterial meningitis, cerebrospinal fluid analysis showed elevated mean WBCs with neutrophilic predominance, elevated protein, and low normal mean glucose. Blood tests showed elevated WBC counts, with neutrophilic predominance (see table 2).

For presumed *Mycoplasma pneumoniae* meningitis, CSF analysis showed a mildly elevated mean WBC (33.3±41.8 WBC/µL, range 0-99) with lymphocytic predominance (43.3±44% lymphocytes, 3.1±3.8% neutrophils), mildly elevated protein (77.7±38.9 mg/dL) and normal glucose levels (72.1±13.9mg/dL). Blood tests showed mildly elevated WBC counts (13.4±5.6x103/µL), with neutrophilic predominance (67.8±19.4% neutrophils, 22±15.4% lymphocytes). CRP was done in 43 cases (51.8%) and 36 (86%) had elevated results.

Computed tomography scan was the most commonly used imaging modality (59.5%), followed by ultrasound (21.6%) and MRI (17.6%). The most common abnormalities found on CT scan were leptomeningeal enhancement (31.8%), subdural effusion (18.2%), infarct (15.9%) and hydrocephalus (15.9%). Leptomeningeal enhancement (23.1%) and infarct (23.1%) were the most common MRI findings. Hydrocephalus was seen in 62.5% of cases where ultrasound was done. CT scan and MRI results were normal in 22.7% and 23.1%, respectively.

The most common complication of bacterial meningitis was recurrent seizures (36.5%), followed by hydrocephalus (14.9%) and subdural effusion (13.5%).

The most commonly used antibacterial agents were ceftriaxone (24.3%), penicillin G (14.9%) and chloramphenicol (13.5 %). Combination therapy was more common in the neonatal age group, where cefuroxime-amikacin and cefotaxime-amikacin were started in 33.3% and 13.3% of cases respectively. Once the diagnosis of meningitis was evident, cefuroxime-amikacin was shifted to the following antimicrobials: meropenem (40%), cefotaxime (20%) , ampicillin (20%) or a combination cefipime-amikacin (20%) Corticosteroids was used in 31.1% of cases.

The mean length of hospital stay was 18.3 days. Majority (54.1%) of patients were fully recovered upon discharge, while 31.1% were

discharged with neurologic deficits, the most common of which were weakness (6.8%), developmental delay (6.8%), seizure disorder (5.4%), hearing loss (4.1%) and lateral rectus palsy (4.1%).

Viral Meningitis

For viral meningitis, one (2.9%) case of Herpes simplex virus (HSV) infection was confirmed by CSF PCR. Majority (97.1%) of cases were not microbiologically confirmed.

Seven (20.6%) cases of presumed HSV 1 or 2, and one (2.9%) case of presumed dengue meningitis were recognized based on compatible clinical and laboratory findings and positive HSV-1 or -2 and dengue virus IgM and IgG serology, respectively. One case of presumed measles (2.9%) and mumps (2.9%) meningitis was identified based on clinical manifestations. There was one (2.9%) presumed Epstein-Barr virus case that manifested with prolonged fever of two weeks, weakness, loss of speech, headache and a positive EBV IgG serology.

Fever, with a mean duration of 5.52 ± 4.91 days, was seen in all cases (100%). Other associated symptoms were seizures (44.1%), headache (44.1%), neck stiffness (23.5%) and cranial nerve palsies (20.6%), with cranial nerves VI and VII being the most commonly involved.

CSF analysis showed a slightly elevated mean WBC and protein with lymphocytic predominance, with normal mean glucose findings. CBC showed a normal WBC (see table 2). C-reactive protein (CRP) was done in 15 (44.1%) cases and only 5 (33.3%) had elevated levels.

CT scan and MRI were done in 47.1% and 32.4% of cases respectively. CT scan was normal in 81.3% of cases. The most common CT scan abnormality was leptomeningeal enhancement (18.8%). The most common MRI findings as described were hyper intensities (36.4%), meningoencephalitis/encephalitis (27.3%) and leptomeningeal enhancement (18.2%). Cranial ultrasound was done in 3 (8.8%) cases, with findings of atrophy (100%) and hydrocephalus (33%).

The most common complications were recurrent seizures (20.6%) and weakness (17.7%), acute disseminated encephalomyelitis (ADEM) (11.8%), and pneumonia (11.8%).

The most common antimicrobial agent used was acyclovir (38.2%) followed by ceftriaxone (26.5%), and chloramphenicol (11.8%). Eleven patients (32.4%) received steroids. Antibiotics were started on some cases as empiric treatment until the diagnosis of viral meningitis became evident.

The mean length of hospital stay was 11.9 days. Majority (55.9%) of cases were discharged completely recovered. Residual morbidities noted in 32.4% of patients included seizure disorder (45.5%), spasticity/decorticate posturing (18.2%) and respiratory failure (9.1%).

Tuberculous Meningitis (TBM)

Among 17 TBM cases, only 3 (17.6%) were confirmed by either CSF TB culture or CSF TB PCR. The remaining 82.4% were diagnosed as probable TBM.

The most common manifestations of TBM were fever (100%), neck stiffness (52.9%), seizures (52.9%), headache (47.1%), vomiting (47.1%), cough (41.2%), and a positive Kernig (35.3%) and Brudzinski sign (29.4%). Cranial nerve palsy was seen in 23.5% of cases.

CSF analysis showed an elevated mean WBC with lymphocytic predominance, elevated mean protein, and low normal glucose levels (see table 2). The complete blood count showed normal mean WBC counts with neutrophilic predominance. C-reactive protein determination was done for all, and was elevated in 70.6% of cases.

Fourteen (82.4%) had a CT scan done, with the most common findings being hydrocephalus (71.4%), basal enhancement (50%), and infarct (28.6%). Only one (5.9%) patient had an MRI, which showed hydrocephalus, basal enhancement and

infarct. Three cases (17.6%) had an ultrasound done, showing hydrocephalus.

The most common complications were recurrent seizures (100%) and hydrocephalus (64.7%) and 23.5% of cases needed surgical intervention.

The most common treatment was a combination of isoniazid, rifampicin, pyrazinamide and ethambutol (76.5%). Streptomycin was added to the standard regimen in the rest of the cases (23.5%). Nine cases (52.9%) received steroids.

The mean length of hospital stay was 14.1 days. Eight cases (47.1%) were discharged completely recovered while eight cases (47.1%) went home with residual morbidity, the most common of which were weakness (17.7%) and lateral rectus palsy (11.8%).

Fungal Meningitis

Two patients had confirmed fungal meningitis where *Cryptococcus neoformans* and *Candida parapsilosis* were isolated.

Fever was the most common clinical manifestation (100%), followed by headache (50%), vomiting (50%), cranial nerve palsies (50%) and weakness (50%).

Cerebrospinal fluid findings showed elevated mean WBCs with 17±17% lymphocytes, 4±4% neutrophils, elevated protein, and markedly decreased glucose. The mean blood WBC was normal, with neutrophilic predominance (see table 2). CRP was elevated in both cases.

MRI was done in one case (50%), and showed restricted diffusion of the posterior-superior parietal cortical regions, with a consideration of encephalitic changes. The complications noted were subdural effusion (50%) and pneumonia (50%). Fluconazole (50%) and amphotericin B (50%) were used in these cases. Methylprednisolone was used in one patient (50%). The mean length of admission was 20 days. Both patients were discharged with residual neurologic morbidity, such as weakness (4/5 MMT on all extremities in 50% of cases) and diplopia (50%).

Fever Duration and Etiology

The Kruskal-Wallis Test results showed that at least two etiologies differed in the median fever duration in days (p=0.0001). Based on Dunn's Test, the median fever duration for viral meningitis cases was statistically shorter than those with TB and longer than those with bacterial meningitis (p=0.0001 and 0.0195, respectively). Furthermore, the median fever duration of TBM cases was statistically longer than those with bacterial meningitis (p<0.0001).

Fungal meningitis, due to its small sample size, was excluded in this and in other subsequent analyses.

Length of Hospital Stay

The Kruskal-Wallis Test results showed that at least two etiologies differed in the median length of stay (LOS) (p= 0.0008). Based on Dunn's Test, the median LOS for viral meningitis was statistically shorter than those with TB and bacterial meningitis (p=0.0127 and 0.0001, respectively). The difference in the median LOS for TB and bacterial meningitis cases was not statistically significant (p=0.3374).

Mortality Rate

The overall mortality rate was 10.2%. The mortality rates for bacterial and viral meningitis were 12.2% and 11.2%, respectively. No mortalities were seen for fungal and TB meningitis.

**DISCUSSION**

Male predilection and the first peak at 1 to 11 months of age observed in this study mirror the national demographics[15]. The second age peak at 5 to 10 years, which was common for viral and probable *Mycoplasma pneumoniae* infections, may be secondary to increased exposure to infectious agents coincident with school entry[16]. The WHO, PCMC and this study's findings are comparable, with 80%[17,] 87.5%[18]and 80% of all Hib meningitis cases

found in children less than 1-year-old. In this study, all cases of Salmonella infection occurred in children under 1 year old, similar to the findings of Owusu-Ofari (2003), who reported that 89.7% of Salmonella spp meningitis cases occurred in infants less than one year.[19] This study's finding of neonatal meningitis being due to gram-negative bacilli in 66.7% and gram-positive cocci in 33.3% of cases is similar to that reported by Morelos and Gatchalian, in which 70% of the pathogens were gram-negative bacilli and 30% were gram-positive cocci[20]. Neonates are particularly vulnerable to gram-negative infections, as neonatally-produced IgMs and maternally transmitted IgGs are less efficient against these organisms[3,16]. Mycobacterium tuberculosis infections are most likely to progress to disease in children younger than five years old, with the risk for disseminated disease being highest in infants.[8]

There was only one (2.9%) laboratory-confirmed case of HSV meningitis identified in this study. Laboratory confirmation of viral meningitis requires either the CSF culture or the viral PCR to be positive. The former has a low sensitivity (<10%)[21] while the latter was not available in the earlier years of this study's duration.

Fever was frequently present across etiologies, and was significantly longer in TB compared to bacterial and viral meningitis. A sub-acute to chronic clinical course and cranial nerve palsies were seen more often in tuberculous infection[22]. The neonates in this study presented with non-specific signs and symptoms, congruent with the findings of a local retrospective study by Morelos and Gatchalian[20].These underscores the need for prompt lumbar puncture and CSF analysis for this subset.

In this study, pleocytosis was highest in bacterial meningitis with CSF WBC counts as high as 12,960/µL. Taken in combination with CSF neutrophilic predominance, a bacterial cause should be highly suspected[23,24].

CSF protein may be elevated in any inflammation or infection caused by any organism, but is usually more elevated in bacterial and TB meningitis, as seen in this study. CSF protein elevation in TBM may be more pronounced due to blood brain integrity breach and gamma globulin synthesis on site[25].

One of the most frequently documented neuroimaging finding in this study was hydrocephalus, which when acquired, is most commonly caused by meningitis[26]. The combination of basal enhancement, hydrocephalus and infarct is specific for TBM[8] similar to the findings of Paguia et. al (2011)[27].

Ceftriaxone as monotherapy was the most commonly used drug in this study. Ceftriaxone constitutes the standard empiric therapy for community-acquired bacterial meningitis as it covers for *Streptococcus pneumoniae*, *Hemophilus influenzae* type b, *Neisseria meningitidis* and Salmonella spp. A local study by Saiton, Jr. (2004) compared ceftriaxone to ampicillin and chloramphenicol for the treatment of Hib meningitis. Patients treated with ceftriaxone had a 62% cure rate compared to 33% and 89% for ampicillin and chloramphenicol respectively. The lowest resistance was seen with ceftriaxone (<10%) and chloramphenicol (<10%), when compared to ampicillin (31%)[18].

Steroids, particularly dexamethasone was used in majority of cases in this study. A Cochrane trial on dexamethasone demonstrated that its use reduced the risk of severe hearing loss (6% from 9.3%), any hearing loss (13.8% from 19%), and neurologic sequelae (17.9% from 21.6%) signficantly[28]. It specifically impacted hearing loss in Hib infections in high-income countries, and decreased the mortality rate for *Streptococcus pneumoniae* and TBM by 6.1% and 25%, respectively[28,29].

Across all etiologies, recurrent seizures were the most common complication documented in this

study. The most common early neurologic complications of bacterial meningitis were seizures (36.5%), hydrocephalus (13.9%) and subdural effusion (13.5%)[30]. These findings were similar to those of Namani et. al. (2012), where subdural effusion was the most common complication of bacterial meningitis, followed by seizures and hydrocephalus[30]. In this study, hydrocephalus was present in 64.7% of children with TBM. This was similar to the findings of Raut (2013) who reported hydrocephalus in about 65% of patients and was associated with a worse prognosis[31].

This study showed no mortality for TB and fungal meningitis. This is contrary to reports from a local and an Indian government tertiary hospital, where mortality rates of 16-23.4% were seen in TBM[8,32]. The private, full-service, tertiary care setting where this study was done might have contributed to the lower mortality rates. The mortality rate for bacterial meningitis was 12.2%, which was close to the findings of Penaflorida and Garcia in 2012.[33]

## CONCLUSION AND RECOMMENDATION

The different types of meningitis shared common symptomatology, including fever, seizures, vomiting, headache and neck stiffness. TBM, however, had the longest fever duration with the most frequent cranial nerve involvement. In bacterial meningitis, CSF pleocytosis was marked except for presumed *Mycoplasma pneumoniae* infection, which had a low mean WBC. The combined findings of leptomeningeal enhancement, hydrocephalus and infarct were unique to TBM. Ceftriaxone was the most commonly used antibiotic for bacterial meningitis, except for neonates for whom the combination of cefuroxime-amikacin was the most common initial regimen used, until microbiologic confirmation was available. Acute disseminated encephalomyelitis (ADEM) was unique to viral meningitis, while hydrocephalus was was more frequent and more severe in TBM. The shortest hospital stay and the highest full recovery rate were seen in viral meningitis.

Epidemiological, clinical and ancillary findings, when taken together, provide important clues to the pathogen and subsequent appropriate treatment for suspected pediatric meningitis cases.

A limitation of this study is the completeness and correctness of first-hand data which were dependent on clinician's entries in the reviewed charts, and which were not uniformly consistent in quality and quantity. Despite this, the setting in which the study was conducted, being a tertiary hospital with a high-volume of patients, makes its findings generalizable to a greater population. The researcher recommends further exploration of specific findings generated from this study.

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