Assessment of the Data of Pediatric Patients with Acute Bacterial Meningitis: 5 years experience

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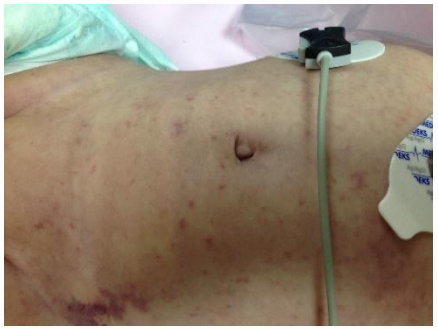

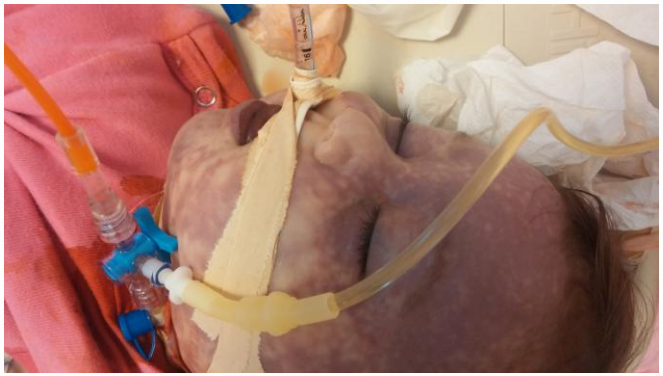

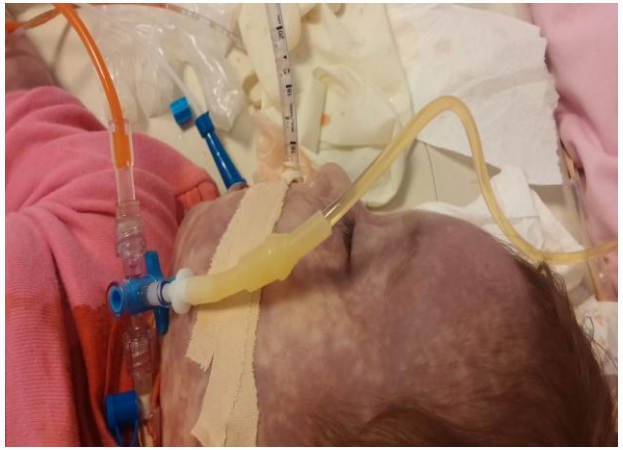

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SEARCH

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Bacterial Meningitis

Language: English (US)

Español: Meningitis bacteriana

Bacterial meningitis is very serious and can be deadly. Death can occur in as little as a few hours. Most people recover from meningitis. However, permanent disabilities (such as brain damage, hearing loss, and learning disabilities) can result from the infection.

There are several types of bacteria that can cause meningitis. Leading causes in the United States include

- *Streptococcus pneumoniae*
- Group B *Streptococcus*
- *Neisseria meningitidis*
- *Haemophilus influenzae*
- *Listeria monocytogenes*

On average, bacterial meningitis caused about 4,100 cases and 500 deaths in the United States each year between 2003 and 2007.[1]

These bacteria can also be associated with another serious illness, sepsis. Sepsis is the body's overwhelming and life-threatening response to infection that can cause tissue damage, organ failure, and death.

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Causes

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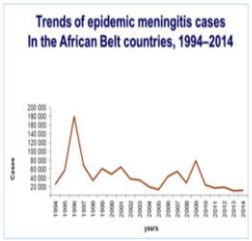
Meningococcal meningitis



Epidemics of meningococcal meningitis: Every year, bacterial meningitis epidemics affect more than 400 million people living in the 26 countries of the extended "African meningitis belt" (from Senegal to Ethiopia). In this area over 900 000 cases were reported in the last 20 years (1995–2014). Of these cases, 10% resulted in deaths, with another 10–20% developing neurological sequelae. The most recent large-scale epidemic in the Belt occurred in 2009 and affected mainly Nigeria and Niger, causing over 80 000 reported cases. From 2010 to 2014 cases have been steadily decreasing, with approximately 24 000 cases in 2010 to 11 500 cases in 2014.

View full size graph
jpg, 71kb


Number of suspected meningitis cases and deaths reported


Vaccine distribution

Contact us

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Number of meningitis epidemics

Introduction

- Bacterial meningitis is a very serious and deadly disease that can be found all over the world despite the existence of suitable treatments.[1, 2]

- It is estimated that over 1.2 million cases suffer from bacterial meningitis each year. [3]

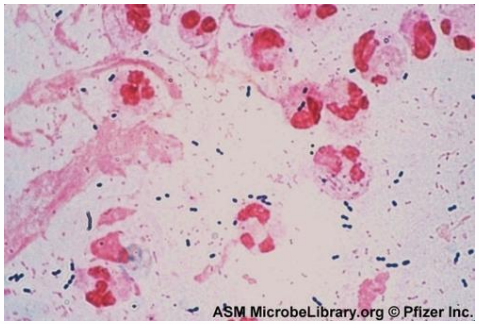
Introduction

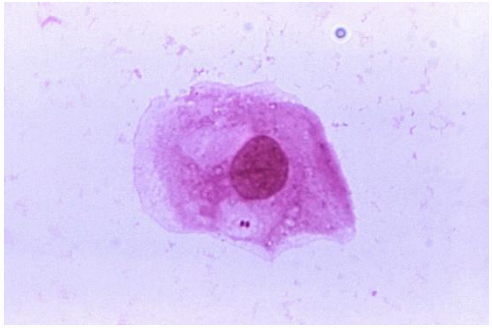
- The most common causes of bacterial meningitis are

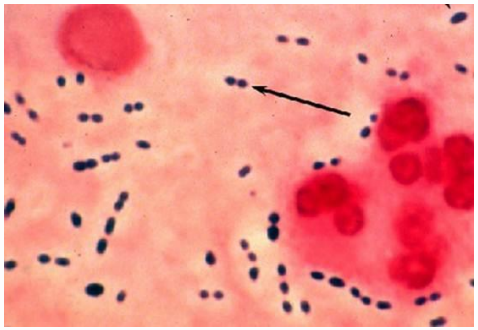
Neisseria meningitidis (N. meningitidis),

Streptococcus pneumoniae (S. pneumococcus)

Haemophilus influenzae type b (Hib).[3]







Introduction

- Pneumococcal, meningococcal and *Haemophilus influenzae type b* vaccines have changed the epidemiology of meningitis.
- Despite a decrease in the incidence of meningitis caused by these agents, *S. pneumoniae* and *N. meningitidis* are still the most frequent causative pathogens of bacterial meningitis beyond the neonatal age in developed countries.[2]


Turkey
TR

Turkish national vaccination schedule

Vaccines	Birth	1 month	2 month	4 month	6 month	12 month	18 month	24 month	4-6 years	11-12 years
Hepatitis B	I	II			III					
Bacille Calmette-Guérin			I							
Diphtheria Tetanus Pertussis Inactivated Poliovirus Haemophilus influenzae type b			I	II	III		Booster			
Pneumococcal			I	II	III	Booster				
Rubella Mumps Measles						I			Booster	
Diphtheria Tetanus Pertussis Inactivated Poliovirus									Booster	
Oral poliovirus					I		II			
Tetanus Diphtheria										Booster
Hepatitis A							I	II		
Varicella						I				

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Meningitis caused by Neisseria Meningitidis, Hemophilus Influenzae Type B and Streptococcus Pneumoniae during 2005–2012 in Turkey

Mehmet Ceyhan, Nezahat Gürler, Yasemin Ozsurekci, Melike Keser, Ahmet Emre Aycan, Venhar Gurbuz, Nuran Salman, Yildiz Camcioglu, Ener Cagri Dinleyici, Sengul Ozkan, Gulnar Sensoy, Nursen Belet, Emre Alhan, Mustafa Hacimustafaoglu, Solmaz Celebi, Hakan Uzun, Ahmet Faik Oner, Zafer Kurugol, Mehmet Ali Tas, Denizmen Aygun, Eda Karadag Oncel, Melda Celik, Olcay Yasa, Fatih Akin & Yavuz Coşkun

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To link to this article: http://dx.doi.org/10.4161/hv.29678

Human Vaccines & Immunotherapeutics

Table 1. Distribution of causative agents of bacterial meningitis and meningococcal serogroups per year in Turkey

Study Period (Year)	2005–2006		2007–2008		2009–2010		2011–2012		2005–2012	
Causative Bacteria	n	%	n	%	n	%	n	%	n	%
Serogroup W-135	59	42.7	19	17.6	23	56.1	26	56.5	127	38.1
Serogroup B	43	31.1	38	35.1	3	7.3	3	6.5	87	26.1
Serogroup A	1	0.8	9	8.3	15	36.6	3	6.5	28	8.4
Serogroup C	0	0	0	0	0	0	0	0	0	0
Serogroup Y	3	2.2	0	0	0	0	0	0	3	0.9
Nongroupable	32	23.2	42	39	0	0	14	30.5	88	26.4
N. meningitidis (Total)	138	56.8	108	40.4	41	62.1	46	66.6	333	51.6
S. pneumonia	55	22.6	98	36.7	21	31.8	21	30.4	195	30.2
H. influenzae type b	50	20.6	61	22.8	4	6.1	2	2.9	117	18.1
Total number of Positive Samples	243	100	267	100	66	100	69	100	645	100
Total number of Evaluated Clinical Samples	408	NA	372	NA	355	NA	317	NA	1452	NA

Turkey, Human Vaccines & Immunotherapeutics, 10:9, 2706-2712, DOI: 10.4161/hv.29678

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RESEARCH PAPER

Bacterial agents causing meningitis during 2013–2014 in Turkey: A multi-center hospital-based prospective surveillance study

Mehmet Ceyhan[a,#], Yasemin Ozsurekci[a,#], Nezahat Gürler[b,#], Eda Karadag Oncel[a,#], Yıldız Camcioglu[c,#], Nuran Salman[d,#], Melda Celik[e,#], Melike Keser Emiroglu[f,#], Fatih Akin[g,#], Hasan Tezer[h,#], Aslinur Ozkaya Parlakay[i,#], Nilden Tuygun[j,#], Diyar Tamburaci[k,#], Ener Cagri Dinleyici[l,#], Adem Karbuz[m,#], Ünal Uluca[n,#], Emre Alhan[o,#], Ümmühan Çay[o,#], Zafer Kurugol[p,#], Nevin Hatipoğlu[q,#], Rengin Şiraneci[q,#], Tolga İnce[r,#], Gülnar Sensoy[s,#], Nursen Belet[s,#], Enes Coskun[t,#], Fatih Yilmaz[t,#], Mustafa Hacimustafaoglu[u,#], Solmaz Celebi[u,#], Ümit Celik[v,#], Metehan Ozen[w,#], Aybüke Akaslan[w,#], İlker Devrim[x,#], Necdet Kuyucu[y,#], Fatmanur Öz[z,#], Sefika Elmas Bozdemir[aa,#], and Ahu Kara[x,#]

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ABSTRACT

This is an observational epidemiological study to describe causes of bacterial meningitis among persons between 1 month and 18 y of age who are hospitalized with suspected bacterial meningitis in 7 Turkish regions. covering 32% of the entire population of Turkey. We present here the results from 2013 and 2014. A clinical case with meningitis was defined according to followings: any sign of meningitis including fever, vomiting, headache, and meningeal irritation in children above one year of age and fever without any documented source, impaired consciousness, prostration and seizures in those < 1 y of age. Single tube multiplex PCR assay was performed for the simultaneous identification of bacterial agents. The specific gene targets were *ctrA, bex*, and *ply* for *N. meningitidis*, Hib, and *S. pneumoniae*, respectively. PCR positive samples were recorded as laboratory-confirmed acute bacterial meningitis. A total of 665 children were hospitalized for suspected acute meningitis. The annual incidences of acute laboratory-confirmed bacterial meningitis were 0.3 cases / 100,000 population in 2013 and 0.9 cases/100,000 in 2014. Of the 94 diagnosed cases of bacterial meningitis by PCR, 85 (90.4%) were meningococcal and 9 (9.6%) were pneumococcal. Hib was not detected in any of the patients. Among meningococcal meningitis, cases of serogroup Y, A, B and W-135 were 2.4% (n = 2), 3.5% (n = 3), 32.9% (n = 28), and 42.4% (n = 36). No serogroup C was detected among meningococcal cases. Successful vaccination policies for protection from bacterial meningitis are dependent on accurate determination of the etiology of bacterial meningitis. Additionally, the epidemiology of meningococcal disease is dynamic and close monitoring of serogroup distribution is comprehensively needed to assess the benefit of adding meningococcal vaccines to the routine immunization program.

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RESEARCH PAPER

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[a]Department of Pediatric Infectious Diseases, Hacettepe University Faculty of Medicine, Ankara, Turkey; [b]Department of Microbiology and Clinical

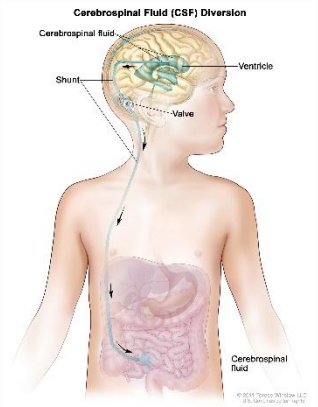
Table 1. Distribution of causative agents of bacterial meningitis and meningococcal serogroups during 2013–2014 in Turkey.

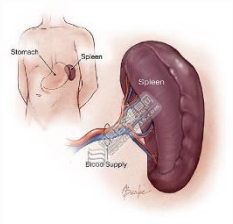
Study Period (Year)	2013		2014		2013–2014 (2 years)	
Causative Bacteria	n	%	n	%	n	%
Serogroup W-135	7	36.8	29	43.9	36	42.4
Serogroup B	5	26.4	23	34.9	28	32.9
Serogroup A	0	0	3	4.5	3	3.5
Serogroup C	0	0	0	0	0	0
Serogroup Y	0	0	2	3.0	2	2.4
Nongroupable	7	36.8	9	13.7	16	18.8
N. meningitidis (Total)	19	86.4	66	91.7	85	90.4
S. pneumonia	3	13.6	6	8.3	9	9.6
H. influenzae type b	0	0	0	0	0	0
Total number of Positive Samples	22	100	72	100	94	100

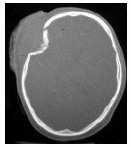
distribution is comprehensively needed to assess the benefit of adding meningococcal vaccines to the routine immunization program.

Introduction

- Certain people are at increased risk of bacterial central nervous system infections and these include



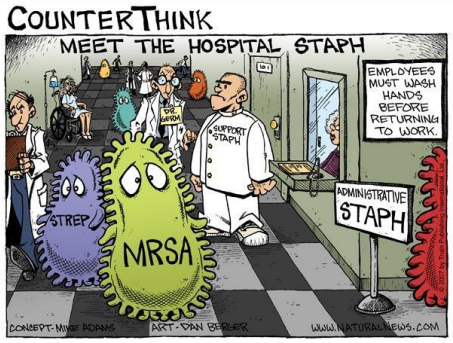




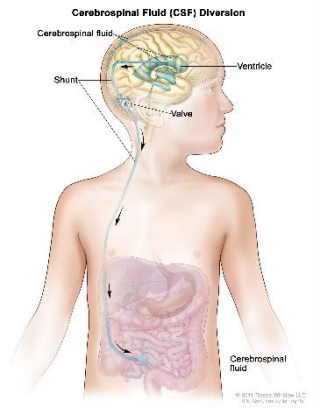
- ✓ Children with immunodeficiency,
- ✓ Newborns and infants,
- ✓ Splenectomy,
- ✓ Human immunodeficiency virus (HIV),
- ✓ Cancer,
- ✓ Immunosuppressive medications,
- ✓ A history of cranial trauma,
- ✓ and
- ✓ Cerebrospinal fluid (CSF) shunt due to hydrocephalus. [2, 4, 5, 6]

Introduction

- Etiological agents may differ in various clinical subgroups.[4]
- In contrast to healthy children, gram-negative bacteria constitute most of the causative agents of nosocomial bacterial meningitis and gram-positive bacteria are common agents in patients with post-neurosurgical meningitis.[7, 8]
- Therefore, recommendations for empirical antibiotic treatment and adjunctive treatments for those clinical subgroups are **different.**[4]

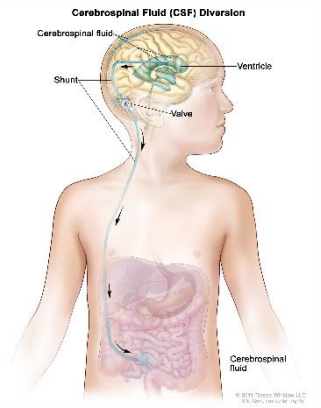


Introduction



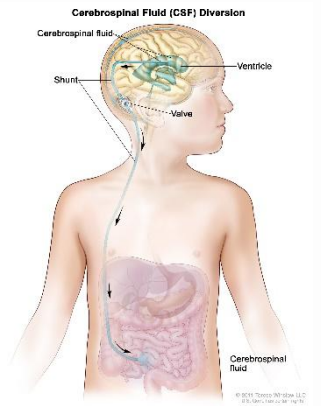
- Hydrocephalus has been known for centuries; however, aseptic surgery, which is the only effective treatment, wasn't applied until the late nineteenth century. [9]
- Then, problems related with CSF shunts such as infection, obstruction, and over drainage have been reported. [10]
- Moreover, infections were found to be responsible for the major mortality and morbidity among patients with CSF shunt.[11]
- Today, more than 100 years after the onset of aseptic surgery, the incidence of CSF shunt infection has changed 1.3-11% [12, 13, 14].

Introduction



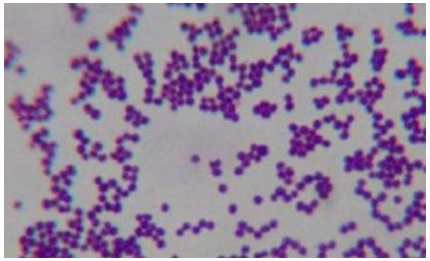
- Annually 33.000 shunt placement procedures are performed in the United States alone and the resulting complications of CSF shunts have been found to be associated with intellectual and neurological deficits and even death.
- As a result, this has lead to high costs.
- It accounts for almost 100 million dollars of national health care expenditure each year. [15]

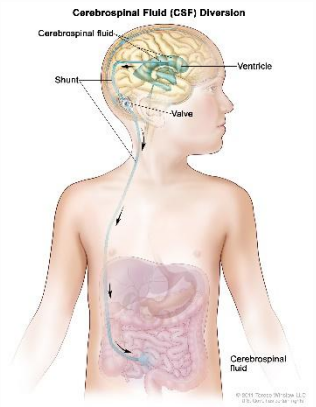
Introduction

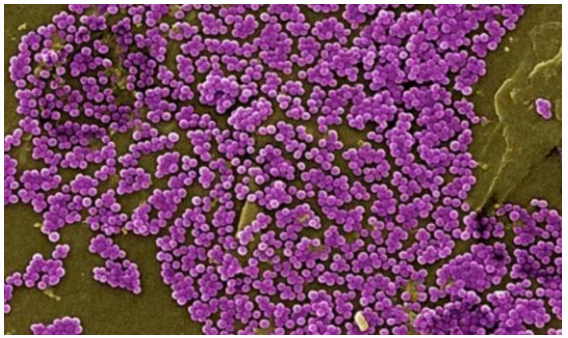


- For this reason the diagnosis and treatment of CSF shunt infection is of great concern in fields such as the neurosurgical, neurological and infectious disease communities. [11]
- Awareness of which infectious agents cause CSF infections in patients with CSF shunt, means that current treatment and prevention methods are essential [13].

Introduction







- *Staphylococcus spp*. is the most common bacterial agent of meningitis in these patients according to literature. [13, 16]

- This is because the infections are commonly caused by colonization of the shunt device by normal nonpathogenic skin flora at the time of surgery. [17]

Introduction

- The aim of our study was

- to investigate the etiological agents of bacterial meningitis in children with or without CSF shunt and the underlying disease and

- to emphasize the importance of immunization, particularly in risk groups.

Materials and Methods
Study group

- We retrospectively analyzed the medical records of patients suspected of having meningitis, who were admitted to our tertiary care hospital between January 2012 and January 2017.

Materials and Methods
Study group

- Inclusion criteria in this study were as follows:

✓ being aged between 1 month and 18 years,

✓ the presence of a clinical image compatible with the diagnosis of meningitis,

✓ laboratory findings including bacterial isolation in CSF samples that was obtained from the CSF shunt or lumbar punction and

✓ having sufficient clinical documentation

Materials and Methods
Study group

- Information recorded included

✓ clinical and demographic characteristics,

✓ medical history,

✓ the presence of medical devices (CSF shunt),

✓ laboratory findings,

✓ The type and antimicrobial susceptibility of the isolated microorganisms,

✓ the length of hospital stay (LOS),

✓ the duration of antimicrobial therapy,

✓ the results of antimicrobial therapy and

✓ prognosis

Definitions

- The clinical case with meningitis was made as follows:

✓any sign of meningitis in children above 1 year of age [fever, vomiting, headache and signs of meningeal irritation],

✓fever without any documented source, impaired consciousness, prostration and seizures in those under 1 year of age. [18]

Definitions

- Isolates evaluated as bacterial contamination were excluded.
- Patients who died during the treatment were included in the assessment as infection-related if the death had been directly caused by the infection. [19]
- The data was collected via patient charts, computerized administrative, pharmaceutical and laboratory databases at Hacettepe University.

Microbiological methods

- Samples which were obtained by lumbar punction or the CSF drainage system were analyzed if CSF had the following criteria:
- 1) >10 leukocytes/mm^3 in the CSF, and/or
- 2) higher CSF protein levels than normal for the patient's age, and/or
- 3) lower CSF glucose levels than normal for their age.
- Additionally, all patients who had positive test results in CSF culture, Gram stain, antigen detection test or polymerase chain reaction (PCR) test were also included.
- Bacteria were identified by **BD Phoenix** (BD Diagnostics System, Sparks, MD) **automated system** used both for identification and antimicrobial susceptibility testing of the isolates between January 2012 and June 2013. Bacteria were identified by matrix-assisted laser desorption ionization–time of flight mass spectrometry (**MALDI-TOF-MS**) and antimicrobial susceptibility testing was performed using the VITEK 2 (bioMérieux, Marcy-l'Étoile, France) system after it had been upgraded in June 2013.

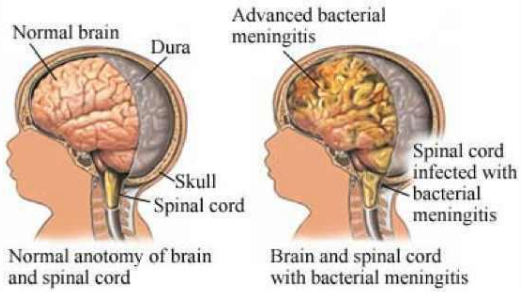
Microbiological methods

- Susceptibility of penicillin, cefotaxime, vancomycin was determined according to the Clinical and Laboratory Standards Institute (CLSI) guidelines. [20]
- Single tube; multiplex PCR assay was performed for the simultaneous identification of bacterial agents.
- The specific gene targets were *ctrA, bex,* and *ply* for N. meningitidis, Hib, and *S. pneumoniae*, respectively. PCR was performed using a DNA thermal cycler

(GeneAmp PCR System model 9700, Applied Biosystems, Foster City, CA, USA).[21]

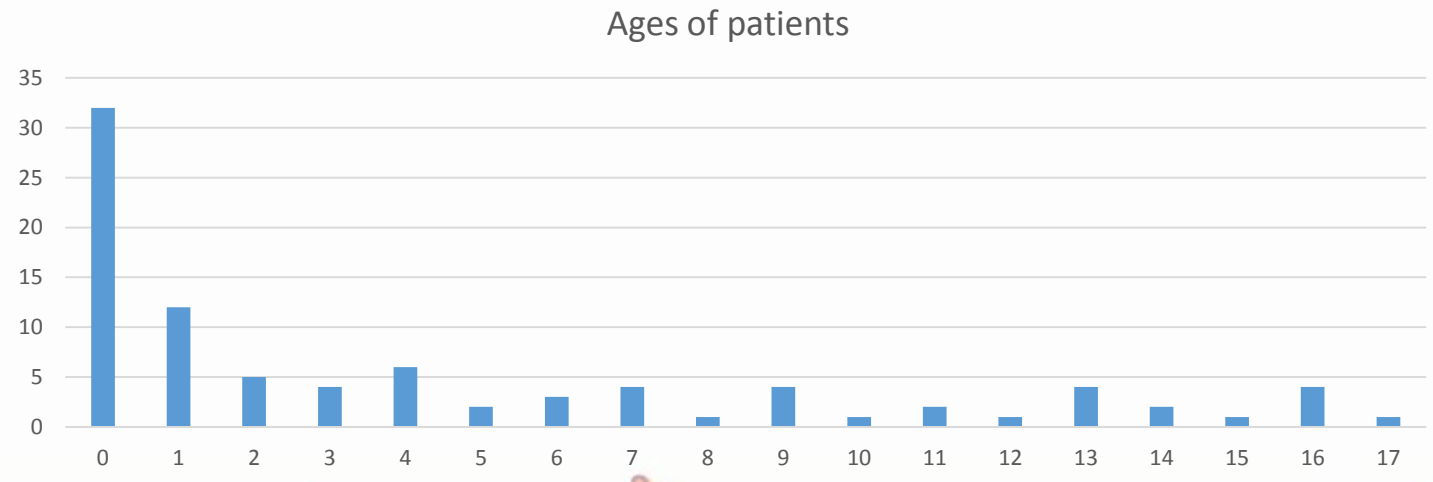
Results

- In total we identified 156 CSF samples in this study and 67 of them were evaluated as being contaminated. The median age of the 89 patients diagnosed with acute bacterial meningitis was 24 months (minimum-maximum; 1-215 months) and the male/female ratio was 49/40.



Results

- The highest frequency of bacterial meningitis was observed in children under the age of 2 with a rate of 50.6% and 67.4% of patients were under the age of 5 (Figure 1).



Results

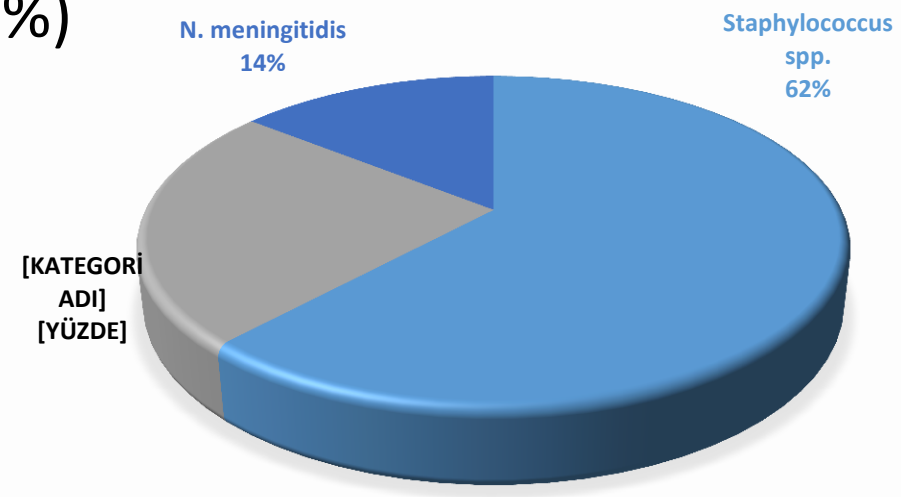
- We evaluated patients in three groups as follows;

1. Patients with CSF shunt [57 (64 %)],
2. Patients with no underlying disease [18 (19.6%)] and
3. Patients with underlying disease [14 (15.7%)] (4 neurological diseases, 3 intracranial tumors, 3 cranial defects, 2 vertebral anomalies, 2 immunodeficiency diseases).

Characteristics	Total cases (n=89)	Patients without underlying disease (n=18)	Patients with CSF shunt (n=57)	Patients with underlying disease (n=14)	p value
Demographics					
Age (months;median:min-max)	24 (1-215)	43 (2-170)	19 (1-215)	26 (2-173)	0.99
Gender (male/female)	49/40	11/7	34/23	4/10	0.09
Bacteria caused meningitis (n, %)					NA
CoNS	32 (36)	0	27 (47.4)	5 (36.7)	
Stapylococcus aureus	7 (7.9)	0	6 (10.5)	1 (7.1)	
Pneumococcus	15 (16.9)	11 (61.1)	3 (5.3)	1 (7.1)	
Meningococcus	9 (10.1)	7 (38.9)	2 (3.5)	0	
E. coli	5 (5.6)	0	2 (3.5)	3 (21.4)	
Mix	3 (3.4)	0	3 (5.3)	0	
Enterococcus spp.	2 (2.2)	0	2 (3.5)	0	
Streptococcus mitis	3 (3.4)	0	2 (3.5)	1 (7.1)	
Acinetobacter spp.	4 (4.5)	0	2 (3.5)	2 (14.3)	
Klebsiella spp.	1 (1.1)	0	0	1 (7.1)	
Pseudomonas spp.	3 (3.4)	0	3 (5.3)	0	
Enterobacter spp.	2 (2.2)	0	2 (3.5)	0	
S. maltophilia	1 (1.1)	0	1 (1.8)	0	
Serratia marcescens	1(1.1)	0	1 (1.8)	0	
Aeromonas sobria	1(1.1)	0	1 (1.8)	0	

Results

- Among all patients, common etiological agents were Staphylococcus spp. (n=39, 43.8%), *S. pneumoniae* (n=15, 16.8%) and *N. meningitidis* (n=9, 10.1%)



Result

Characteristics	Total cases (n=89)	Patients without underlying disease (n=18)	Patients with CSF shunt (n=57)	Patients with underlying disease (n=14)	p value
Demographics					
Age (months;median:min-max)	24 (1-215)	43 (2-170)	19 (1-215)	26 (2-173)	0.99
Gender (male/female)	49/40	11/7	34/23	4/10	0.09
Bacteria caused meningitis (n, %)					NA
CoNS	32 (36)	0	27 (47.4)	5 (36.7)	
Stapylococcus aureus	7 (7.9)	0	6 (10.5)	1 (7.1)	
Pneumococcus	15 (16.9)	11 (61.1)	3 (5.3)	1 (7.1)	
Meningococcus	9 (10.1)	7 (38.9)	2 (3.5)	0	
E. coli	5 (5.6)	0	2 (3.5)	3 (21.4)	
Mix	3 (3.4)	0	3 (5.3)	0	
Enterococcus spp.	2 (2.2)	0	2 (3.5)	0	
Streptococcus mitis	3 (3.4)	0	2 (3.5)	1 (7.1)	
Acinetobacter spp.	4 (4.5)	0	2 (3.5)	2 (14.3)	
Klebsiella spp.	1 (1.1)	0	0	1 (7.1)	
Pseudomonas spp.	3 (3.4)	0	3 (5.3)	0	
Enterobacter spp.	2 (2.2)	0	2 (3.5)	0	
S. maltophilia	1 (1.1)	0	1 (1.8)	0	
Serratia marcescens	1(1.1)	0	1 (1.8)	0	
Aeromonas sobria	1(1.1)	0	1 (1.8)	0	
Laboratory findings (median, min-max)					
CSF protein	126 (13-2940)	71 (13-701)	128 (13-2940)	141 (30-1032)	0.92
CSF glucose	35 (0-124)	20 (0-95)	36 (0-124)	32 (4-73)	0.13
WBC (x1000/uL)	11.6 (2.9-35.5)	10.6 (2.9-30.6)	11.9 (5.9-28.9)	10.6 (3.7-35.5)	0.56
Thrombocyte (x1000/uL)	368 (24-887)	267 (96-715)	409 (53-877)	401 (24-735)	0.02
C-reactive protein	4.4 (1-33)	7.3 (0.1-33)	7.5 (0.4-33)	1.2 (0.1-10)	0.18
Sepsis and/or DIC	10 (11.2)	4 (22.2)	5 (8.8)	1 (7.1)	0.25
Duration of hospitalization	17 (0-189)	10 (0-64)	19 (0-189)	18 (9-91)	0.07
Outcome					
Infectious related mortality	9 (10.1)	1 (5.6)	6 (10.5)	2 (14.3)	0.71
Overall mortality	13 (14.6)	1 (5.6)	9 (15.8)	3 (21.4)	0.41

- Pneumococcal and meningococcal meningitis detected in previously healthy patients with rate of 61.1% and 38.9%, respectively.
- CoNS were the most common causative agents (47.4%) in patients with CSF shunt.

Results

- Pneumococcal PCR tests were positive in 7 patients, pneumococci were detected with culture in 2 patients and both PCR and culture were positive in 6 patients.
- Serotypes could be detected in only four out of 15 patients with pneumococcal meningitis.
- Two of them were non-vaccine serotypes (15B, 15A) and the others were serotype 19F and 1.
- Four of the children with pneumococcal meningitis had been vaccinated only one dosage; the others had been vaccinated with pneumococcal-conjugated vaccine according to our national immunization program.

Results

- There was only one case of culture positive meningococci and 8 cases were diagnosed with meningococci by PCR.

- The serogroups of nine patients with meningococcal meningitis were serotype W for 3, serotype B for 2, and 4 patients of nongroupable.

- None of the children had been vaccinated with meningococcal vaccines or 23-valent pneumococcal vaccines.

Results

- No difference was found between patients in the three groups in terms of age, gender, white blood cell count, C-reactive protein, and duration of hospitalization except for the thrombocyte count.

- The median thrombocyte count in healthy children was $264x10^3/uL$ (min-max; 96-715). This count was lower than among the others and therefore was statistically significant ($p=0.02$).

- Sepsis and/or disseminated intravascular coagulation (DIC) were seen in 22.2% of healthy children; however, only 8.8% in patients with CSF shunt and 7.1% in patients with underlying disease.

Results

- The duration of hospitalization was lower in patients who had previously been healthy than in the other groups. However, this was not statistically important (p=0.07).

- Among these previously healthy patients only one died from meningococcal meningitis.
- The overall mortality rate and infection related mortality were similar between the groups.

Results

- All 8 cultured pneumococcal isolates were susceptible to vancomycin and cefotaxime and 4 were resistant to penicillin.
- One meningococcal isolate was moderately susceptible to penicillin.
- The methicillin resistance rate was 42.8% in *Staphylococcus aureus* isolates and 30.6% in CoNS isolates.
- All *Staphylococcus spp.* isolates were susceptible to vancomycin.

Discussion

- The most common etiological agents were *Staphylococcus* spp, *S. pneumonia, N. meningitidis*, and *E. coli* in a decreasing order in our study.
- Both *Hib* and pneumococcal vaccines were implemented in the national immunization schedule of Turkey in 2006 and 2008, respectively.
- Therefore, a possible etiological shift of bacterial meningitis may be attributable to the vaccination program, consistent with literature.

Characteristics	Total cases (n=89)
Bacteria caused meningitis (n, %)	
CoNS	**32 (36)**
Stapylococcus aureus	**7 (7.9)**
Pneumococcus	**15 (16.9)**
Meningococcus	**9 (10.1)**
E. coli	**5 (5.6)**
Mix	3 (3.4)
Enterococcus spp.	2 (2.2)
Streptococcus mitis	3 (3.4)
Acinetobacter spp.	4 (4.5)
Klebsiella spp.	1 (1.1)
Pseudomonas spp.	3 (3.4)
Enterobacter spp.	2 (2.2)
S. maltophilia	1 (1.1)
Serratia marcescens	1(1.1)
Aeromonas sobria	1(1.1)

Discussion

- A study from Japan after the widespread use of *Hib* and *S. pneumonia* vaccines for four years, *Streptococcus agalactia, S. pneumonia and E. coli* were detected as main causative bacteria in pediatric bacterial meningitis. [32]

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Original Article

Pediatric bacterial meningitis in Japan, 2013–2015 – 3–5 years after the wide use of *Haemophilus influenzae* type b and *Streptococcus pneumoniae* conjugated vaccines☆

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ABSTRACT

Background: *Haemophilus influenzae* type b (Hib) vaccine and pneumococcal conjugated vaccine (PCV) have been widely used since 2010 in Japan when both vaccines were supported by the regional governments, and they were covered as routine recommended vaccines in 2013. The incidence of bacterial meningitis due to these organisms decreased in 2011 and 2012, but meningitis due to *Streptococcus agalactiae* and *Escherichia coli* remained unchanged.
Objectives: We planned to confirm whether the incidence also decreased in subsequent years.
Methods: We analyzed the epidemiological and clinical data for 2013–2015, and compared the information obtained in the previous nationwide survey database and our previous reports. We also investigated the risk factors for disease outcome.
Results: In the 2013–2015 surveys, 407 patients from 366 hospitals from all prefectures were evaluated. *S. agalactiae* (33%), *Streptococcus pneumoniae* (25%), and *E. coli* (10%) were the main organisms. The total number of patients hospitalized with bacterial meningitis per 1000 admissions decreased from 1.19 in 2009–2010 to 0.37 in 2013–2015 ($p < 0.001$). The incidence of *H. influenzae* and *S. pneumoniae* meningitis significantly decreased from 0.66 in 2009–2010 to 0.01 in 2013–2015, and from 0.30 to 0.09, respectively ($p < 0.001$). Only 0–2 cases with *Neisseria meningitidis* were reported each year throughout 2001–2015. The fatality rates for *H. influenzae*, *S. pneumoniae*, *S. agalactiae*, and *E. coli* in 2013–2015 were 0.0, 4.1, 3.1, and 2.6%, respectively. Risk factors for death and sequelae were consciousness disturbance, convulsion, low CSF glucose, and *Staphylococcus* sp. as a causative organism ($p < 0.01$).
Conclusions: Hib vaccine and PCV have decreased the rate of bacterial meningitis. *S. agalactiae* has subsequently become the most common cause of bacterial meningitis in Japan.

Discussion

- In another study from Pakistan, CoNS and *S. pneumoniae* were common pathogens in children with acute bacterial meningitis. [35]
- It is obvious that vaccines have reduced the incidence of meningitis worldwide despite changes in bacterial meningitis epidemiology [25, 34, 35].

Childhood Acute Bacterial Meningitis: Clinical Spectrum, Bacteriological Profile and Outcome

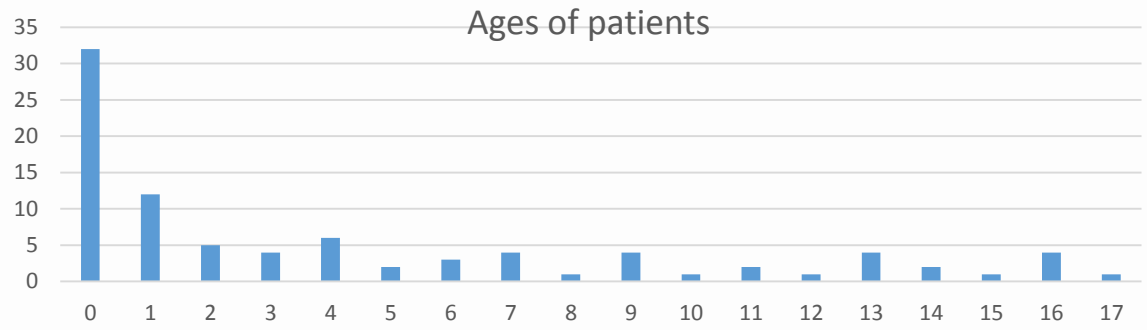
Attia Bari[1], Fatima Zeeshan[1], Aiza Zafar[2], Hassan Ejaz[2], Aisha Iftikhar[1] and Ahsan Waheed Rathore[1]

ABSTRACT

Objective: To determine the disease pattern, etiological agents and outcome of childhood acute bacterial meningitis.
Study Design: A descriptive study.
Place and Duration of Study: Department of Paediatric Medicine, The Children's Hospital, Lahore, from January to December 2012.
Methodology: A total of 199 children between the ages of 1 month and 5 years, admitted with the diagnosis of meningitis on the basis of clinical findings and positive cerebrospinal fluid (CSF), were included. In all patients, complete blood count (CBC), CSF culture sensitivity, and blood culture sensitivity were performed. Data was analysed using SPSS version 20.
Results: Out of 199 children, 127 (63.8%) were males with M:F ratio of 1.7:1. Mean age was 11.33 ±12 months. Maximum numbers of children were < 1 year of age, 136 (68.3%). Only 90 (45.2%) children were fully vaccinated according to Expanded Program of Immunisation (EPI) schedule. Presentations with refusal to take feed (p=0.008) and with impaired conscious state were independent predictors of death (p=0.002). Complications were noted in 34 (17%) and were significantly associated with severe malnutrition (p=0.006) and altered conscious level at presentation (p < 0.001). The common pathogens identified on CSF culture were *coagulase negative staphylococci* (CoNS) in 11 (5.5%) and *streptococcus pneumoniae* in 5 (2.5%). Overall mortality was 10.1%. The commonest pathogen isolated from children who died was *streptococcus pneumoniae* (p=0.039).
Conclusion: Acute bacterial meningitis mostly affected children under the age of 1 year. CSF culture revealed both Gram-positive and Gram-negative bacteria. The most common pathogen in children who died was streptococcus pneumoniae.

Discussion

- In the present report, most of the affected children were under 2 years of age in accordance with other studies in literature [27,28].



Discussion

- In this study, only pneumococcal and meningococcal meningitis were detected in previously healthy patients with rates of 61% and 38.9%, respectively.
- One patient with immunodeficiency and three patients with CSF shunt were also diagnosed with pneumococcal meningitis.
- Two patients with CSF shunt were diagnosed with meningococcal meningitis.

Characteristics	Total cases (n=89)	Patients without underlying disease (n=18)	Patients with CSF shunt (n=57)	Patients with underlying disease (n=14)
Bacteria caused meningitis (n, %)				
CoNS	32 (36)	0	27 (47.4)	5 (36.7)
Stapylococcus aureus	7 (7.9)	0	6 (10.5)	1 (7.1)
Pneumococcus	15 (16.9)	11 (61.1)	3 (5.3)	1 (7.1)
Meningococcus	9 (10.1)	7 (38.9)	2 (3.5)	0
E. coli	5 (5.6)	0	2 (3.5)	3 (21.4)
Mix	3 (3.4)	0	3 (5.3)	0
Enterococcus spp.	2 (2.2)	0	2 (3.5)	0
Streptococcus mitis	3 (3.4)	0	2 (3.5)	1 (7.1)
Acinetobacter spp.	4 (4.5)	0	2 (3.5)	2 (14.3)
Klebsiella spp.	1 (1.1)	0	0	1 (7.1)
Pseudomonas spp.	3 (3.4)	0	3 (5.3)	0
Enterobacter spp.	2 (2.2)	0	2 (3.5)	0
S. maltophilia	1 (1.1)	0	1 (1.8)	0
Serratia marcescens	1(1.1)	0	1 (1.8)	0
Aeromonas sobria	1(1.1)	0	1 (1.8)	0

Discussion

- Ten out of 15 patients with pneumococcal meningitis were detected in the first year after the onset of pneumococcal conjugate vaccine-13 vaccination, where the effects of the vaccination had still not been seen.

Discussion

- Our five-year experience with this study demonstrated that we had no *Hib* meningitis either in patients with underlying diseases or in patients with CSF shunt due to the success of *H. influenza* vaccination which was included in the primary immunization schedule in 2006. [26]

- Additionally, it is important to recommend that children with CSF shunt receive a 23-valent-polysaccharide pneumococcal vaccine.[5] No patient in our study had received this vaccine.

Discussion

- The epidemiological agents were different in patients with underlying disease; CoNS (36.6%) and E. coli (21.4%) were the most common causative agents in this group.

- In previous reports, consistent with the present results, it was stated that the characteristics of patients who had nosocomial infections, neurosurgical treatment and immunodeficiency were different when compared with those patients who had no underlying disease. [4, 7, 29, 30, 29]

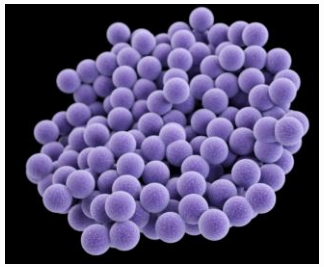
Characteristics	Patients with underlying disease (n=14)
Bacteria caused meningitis (n, %)	
CoNS	5 (36.7)
Stapylococcus aureus	1 (7.1)
Pneumococcus	1 (7.1)
Meningococcus	0
E. coli	3 (21.4)
Mix	0
Enterococcus spp.	0
Streptococcus mitis	1 (7.1)
Acinetobacter spp.	2 (14.3)
Klebsiella spp.	1 (7.1)
Pseudomonas spp.	0
Enterobacter spp.	0
S. maltophilia	0
Serratia marcescens	0
Aeromonas sobria	0

Discussion

- CSF shunts, which lead to increased meningitis incidence, are another important factor in changing bacterial meningitis epidemiology [2, 12] and are commonly used worldwide for the treatment of hydrocephalus [31, 9].

- In children who undergo CSF shunting procedures, infection is a major cause of mortality (10-13%) [11, 36]. In our study, infection related mortality was 10.2% in patients with CSF shunt.

Discussion



- Staphylococcal species are a common cause of shunt-related infection.
- Consistent with our findings, the most frequent bacteria is CoNS and the second is *Staphylococcus aureus* in patients with shunt related infections. [12, 14, 16, 36]
- Three patients had pneumococcal and two patients had meningococcal meningitis in this group. Recently, few pediatric cases with CSF shunt have been diagnosed with pneumococcal meningitis. [5, 38, 39]

Discussion

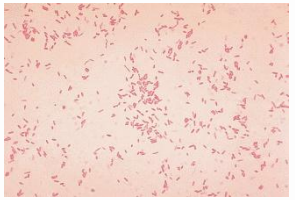
- Additionally, the present study is one of the few reports about *N. meningitidis* associated CSF shunt infection in children in literature.

- Firstly, an 11-month-old male with ventriculoperitoneal shunt was reported in 1984. *N. meningitidis* serotype C was recovered from the CSF culture of this patient and he was treated with penicillin G for 14 days and discharged in healthy condition [40].

Discussion

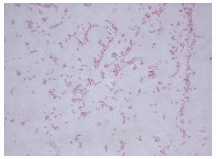
- In our study, there were two children with meningococcal shunt infection, one of whom was a 15 month-old male and meningococcus W serotype was detected by PCR; however, *Pseudomonas aeruginosa* was detected in CSF culture. He was treated with meropenem and ciprofloxacin for 4 weeks and his shunt was revised.
- The other patient was a 19 month-old female, and she had nongroupable meningococcal meningitis, which was confirmed in CSF via PCR. Vancomycin and cefotaxime treatments were applied for ten days without revision of her shunt. Both patients recovered.

Discussion



- *Aeromonas sobria,* is a gram-negative small bacilli, and to our knowledge has not been reported before as a meningitis agent in patients with CSF shunt. Aeromonas species are isolated from a variety of environmental sources including water, seafood, meat and vegetables. [41]
- The clinical spectrum of Aeromonas spp. infection in humans is acute gastroenteritis, hepatobiliary tract infection, peritonitis, pneumonia, empyema, meningitis, septic arthritis, osteomyelitis, endocarditis, bacteremia, burn and wound infection.
- Our patient was a 19-month-old male and *Aeromonas sobria* was isolated in two consecutive cultures. Cefotaxime treatment were given for 14 days.
- The shunt was revised and then he was discharged in a healthy condition.

Discussion



- *Stenotrophomonas maltophilia (S. maltophilia)* is another rare causative agent, which has especially been associated with shunts and drainages. [46] One of our patients had *S. maltophilia* meningitis.
- He was a 7-month-old male with a CSF shunt for hydrocephalus and treated with intravenous ciprofloxacin, trimethoprim-sulfamethoxazole and amikacin, however *S. maltophilia* could not be eradicated.
- According to his antibiotic susceptibility report, antibiotics were changed to levofloxacin, high dose trimethoprim-sulfamethoxazole, and intraventricular amikacin and his shunt was removed. He was discharged after 14 days in a healthy condition.
- Consequently, physicians should be aware of infections due to scarce gram-negative agents in this patient group.

Discussion

- No difference was found between patients with or without CSF shunt in terms of demographic, clinical and laboratory characteristics except for the thrombocyte count. The median thrombocyte count was lower in patients without underlying diseasse.

- This could be attributed to the fact that sepsis and DIC were commonly seen in patients without underlying diseasse. It has also been reported in literature that there is a strong association between sepsis/infection and thrombocytopenia. [47]

Limitations

- There are some limitations to our study.
- First, it was carried out with a single center data.
- Second, there is potential for bias and inaccurate data collection due to retrospective nature of this study.

Conclusion

- The epidemiology of bacterial meningitis continues to shift with the ongoing introduction of conjugated vaccines for the most common meningeal pathogens, particularly type b *H. influenzae* (Hib), pneumococcal and meningococcal vaccines.

- Our study showed that bacterial meningitis etiology is different in patients with or without a CSF shunt.
- Physicians should be aware of and take into consideration both rare and common bacterial agents in childhood meningitis when managing patients with a CSF shunt.

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