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Research Article

Frequency, Distribution and Antibiotic Resistance of Pathogens in the Cerebrospinal Fluid of Children with Meningitis in Pediatric Hospital-Bengazi-Libya

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Abstract

Bacterial meningitis is a fatal, restricting and endemic disease requiring rapid antimicrobial therapy. The aim of this prospective longitudinal study was to document the causative agents in suspected cases of meningitis by performing cultures and rapid tests, their antimicrobial susceptibility profile, and to find its mortality rate from Summer 2017 to Spring 2019. 7276 cerebrospinal fluids (CSF) samples were collected from patients suspected of meningitis in Benghazi Pediatric Hospital of which 146 (2%) were positive bacterial meningitis and 454 (6.24%) were positive viral meningitis. The most common isolated pathogen was Gram negative bacilli 30 (20.5%), followed by *Haemophilus influenzae* 20 (14%), *Streptococcus pneumonia* 18 (12%), *Neisseria meningitides and E. coli* 16 (11%) equally, *Pseudomonas* spp 14 (9.5%), *Staph. albus and Staph. epidermidis* 10 (7%) equally and *Klebsiella* spp and *Staphylococcus aureus* 6 (4%) equally. As many as 50% patients with pneumococcal meningitis also showed evidence of pneumonia on an initial chest radiography. The maximum antibiotic resistance was towards Ampicillin 34 (23.3%) followed by Sulfamethoxazole 32 (21.9%). The low susceptibility was recorded towards Erythromycin 18 (12.32%) and Augmentin 19 (13%). Amikacin 19 (13%) followed by Colistin 18 (12.32%) were recorded to have intermediate susceptibility. Ciprofloxacin 86 (58.9%) followed by Augmentin 53 (36.3%) and Ceftriaxone 48 (32.9%) had the highest antibiotic susceptibility. The majority of cases, 1218 (16.74%), were isolated in Summer 2018, followed by 1017 (13.98%) cases in Spring and Autumn 2018, while the lowest incidence, 334 (4.59%), was observed in Summer 2017. The child begins to improve within 24 to 36 hours after starting antibiotics and 90% of children with bacterial meningitis recover completely with no long-term complications. However, 10% of meningitis cases can damage the brain and cause long-term complications, including deafness, delayed growth or learning difficulties, muscle spasms or paralysis, and seizures (deaths are uncommon), which is the main reason the Libyan Ministry of Health provides free vaccinations against Meningitis for Libyan children from birth until they enter school.

Keywords: *Cerebrospinal Fluid; Antimicrobial Resistance; Meningitis; Pediatric Hospital*

Introduction

Acute bacterial meningitis is one of the primary reasons for death worldwide [1]. Every year, over 1,000,000 patients are affected, with the incidence being greater in developing countries and in specific geographic areas. Infectious diseases are widespread in Egypt; *S. pneumonia* meningitis is currently the predominant cause of meningitis in Egypt and results in the highest number of deaths among meningitis patients, especially below one year of age [2,3]. Differentiating bacterial from viral meningitis is incredibly vital for definitive treatment. Acute meningitis is caused by a range of infectious pathogenic bacteria. Pyogenic bacteria, such as *S. pneumoniae, N. meningitidis* and *H. influenza,* are the most prevalent causes of meningitis respiratory disease [4]. Gram stain smears of the CSF are a rapid and reliable method to identify microorganisms in 60% - 90% of meningitis patients [6]. The CSF culture is a very specific test [5]. The common CSF characteristics in bacterial meningitis are polymorphonuclear leukocytosis, increased protein concentration, and reduced glucose concentration. In viral meningitis, the usual CSF abnormalities are lymphocytic pleocytosis, normal glucose concentration and a normal or slightly elevated protein concentration [7]. Other diagnostic tests used to differentiate between bacterial and viral meningitis are peripheral WBC count, CRP and ESR, which are usually elevated in patients with bacterial meningitis [8].

Objective of the Study

The aim of this prospective observational study is to document the causative agents in suspected cases of meningitis by performing rapid tests and cultures, to evaluate the seasonality of bacterial and viral meningitis, to identify the alarming growth of antibiotic-resistance, and to find the mortality rate in these patients between Summer 2017 and Spring 2019 in Benghazi Pediatric hospital.

Materials and Methods

Study populations

From Summer 2017 to Spring 2019, 7276 cerebrospinal fluid (CSF) samples were collected from patients suspected of meningitis in Benghazi Pediatric Hospital in this prospective observational study. After microscopic examination, samples were cultured for bacterial identification and antibiotic susceptibility.

Laboratory analysis

In general, after a patient's history and physical examination, if meningitis is suspected, a lumbar puncture should be performed promptly. The cerebrospinal fluid (CSF) analysis and culture is the cornerstone in diagnosing meningitis. First, the opening pressure should be measured and, next the fluid should be sent to the lab for cell count (and differential count), chemistry (i.e. CSF glucose and protein), and microbiology (i.e. Gram stain and cultures). In Pediatric hospital- Benghazi, blood cultures are needed to complement the CSF culture.

CFS sample handling

After drawing, the CSF samples are labelled, and the following steps are taken:

1. **Tube 1:** Sent to the chemistry laboratory for glucose and protein:
    a. **Protein:** In the neonate, a CSF protein of > 125 to 150 mg/dL in preterm, and > 100 mg/dL in term infants is consistent with bacterial meningitis.
    b. **Glucose:** The CSF glucose concentration < 30 mg/dL (1.7 mmol/L) in a term infant or < 20 mg/dL (1.1 mmol/L) in a preterm infant is consistent with bacterial meningitis in the neonate.
2. **Tube 2:** Sent to the hematology laboratory for a cell count with differential:

Laboratory features that are characteristic of neonatal bacterial meningitis include:

a. **Abnormal peripheral blood cell counts:** Ex. high or low white blood cell [WBC] count, elevated ratio of immature to total neutrophils, low platelet count.

b. **Abnormal cerebrospinal fluid (CSF) parameters:** Ex. elevated CSF WBC, elevated CSF protein, decreased CSF glucose.

3. **Tube 3:** Sent to the microbiology and immunology laboratory:

a. Cultures of CSF were performed at the Pediatric Hospital Laboratories in Benghazi. When samples were collected, they were transported in trans-isolate medium at ambient temperature to the Pediatric Hospital Laboratories. Sediment from a centrifuged specimen of CSF was cultured on blood agar (BA), MacConkey agar (MA), and vitox-enriched chocolate agar (CA) plates. Plates were incubated for 24 - 48hrs at 35°C in either an aerobic atmosphere (BA and MA), an anaerobic atmosphere (BA), or an incubator at a gas concentration of 5% CO_2 (CA). Isolates from cultures were identified by standard methods. All bacterial isolates were tested for *in vitro* antibiotic disc sensitivity.

Treatment

Antibiotic treatment varied from patient to patient but in most cases Chloramphenicol (100 mg/kg/day parenterally) was the first antibiotic administered. In infants less than one month of age, this was augmented with Gentamicin (5 - 7.5 mg/kg/day). The treatment was given parenterally in all cases for 10-14 days. The antibiotics were used during the study period for all specimens. A-Ampicillin, Co-Cotrimoxazole, AMC-Augmentin, G-Gentamicin, VA-Vancomycin, FD-Fusidic acid, AK-Amikacin, CAR-Carbapenem, E-Erythromycin, CRL-Clarithromycin, Ox-Oxacillin, SXT-Sulfamethoxazole, IMP-Imipenem, AML-Amoxicillin, P-Penicillin G, CN- Cloxacillin, NA-Nalidixic acid, PIP-Piperacillin, CT-Colistin, CIP-Ciprofloxacin and CH-Chloramphenicol, R-Rifampicin, FOX-Cefotaxime, CFX-Ceftriaxone, T-Tetracycline, and CL-Clindamycin were the antibiotics that demonstrated consistently *in-vitro* activity against all cultured organisms.

Results

Seven thousand and two hundred seventy-six (7276) suspected meningitis cases were examined using culture in microbiology laboratory.

Distribution of cases according to the gender

Table 1 and figure 1 illustrate the distribution of the sample items according to gender; 4039 (55.5%) cases were male, while 3237 (44.5%) were female.

Gender	Frequency	Percent
Male	4039	55.5%
Female	3237	44.5%
Total	7276	100%

Table 1: *Comparison between the cases according to gender.*

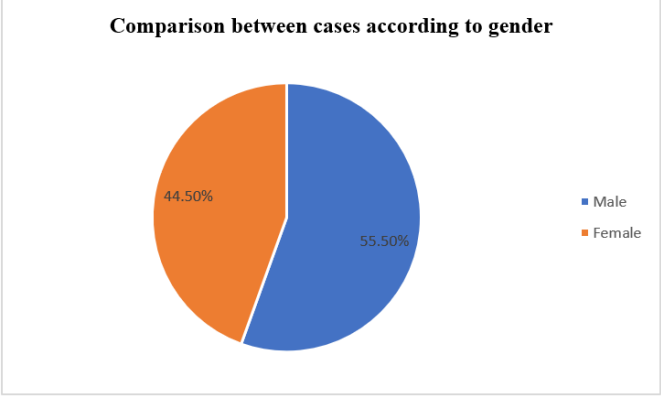

Figure 1: *Comparison between the cases according to gender.*

Distribution of cases according to the age

Age group	Negative cases		Positive cases	
	Percent	Frequency	Percent	Frequency
< 2 months	10%	668	30%	180
< 1 year	6%	400	10%	60
1 - 2 year	20%	1335	10%	60
2 - 3 year	8%	534	5%	30
3 - 4 year	6%	401	5%	30
4 - 5 year	7%	467	5%	30
5 - 6 year	3%	200	5%	30
6 - 7 year	2%	134	5%	30
7 - 8 year	8%	534	5%	30
8 - 9 year	10%	668	5%	30
9 - 10 year	10%	668	5%	30
10 - 15 year	10%	667	10 %	60
Total	100%	6676	100%	600

Table 2: *Age-wise distribution of positive cases against total cases.*

According to the results from our study as shown in table 2, the greatest proportion of positive meningitis cases occurred in the age group between 2 - 10 years, representing 40% of positive cases, followed by 30% of cases less than 2 months of age and 20% of cases between 2 months to 2 years of age. The least number of positive cases were in the age group 11 - 15 years, representing only 10% of positive cases.

Distribution of positive and negative cases for bacterial meningitis at pediatric hospital from summer 2017 to spring 2019

Table 3 and figure 2 demonstrate the number of samples that showed no growth of bacteria, which is 7130, amounting to 98% of all samples, while 146 samples showed growth of bacteria, which represents the remaining 2% of all samples. Bacterial pathogens were isolated from all the 146 (2%) samples that showed growth of bacteria.

Culture	Frequency	Percent
No growth	7130	98%
Growth	146	2%
Total	7276	100%

Table 3: *Distribution of positive and negative cases for bacterial meningitis at Pediatric Hospital from Summer 2017 to Spring 2019.*

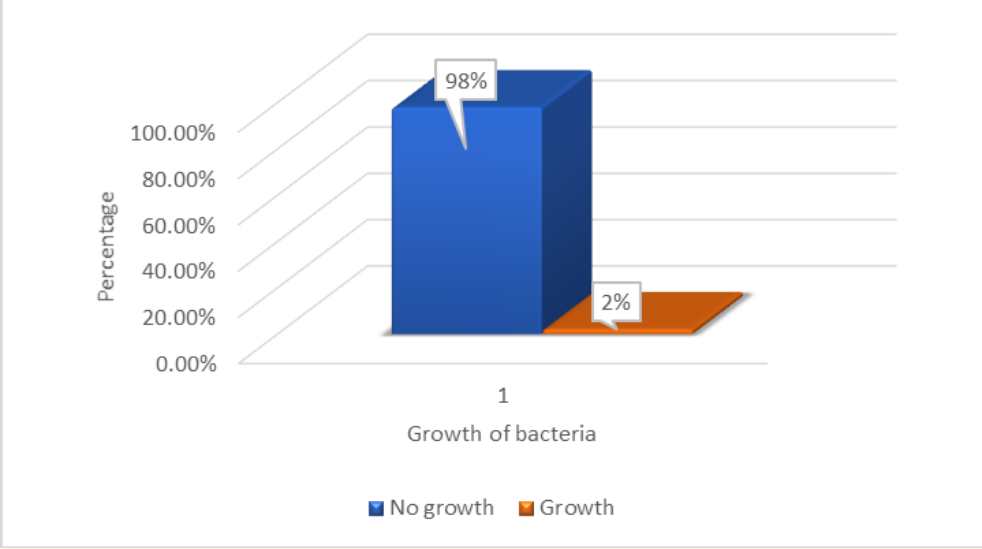

Figure 2: *Distribution of positive and negative cases for bacterial meningitis at pediatric hospital from summer 2017 to spring 2019.*

Place distribution of samples for meningitis patients at pediatric hospital from summer 2017 to spring 2019

Table 4 shows the place distribution of samples for meningitis patients at Pediatric Hospital from Summer 2017 to Spring 2019 and is broken department wise. The place distribution of samples for meningitis at Benghazi Pediatrics Hospital is 22.10% patients admitted in medical department A, 18.80% patients admitted in medical department B, 18.75% patients admitted in medical department C, 12.40% patients admitted in medical department G, 12.64% patients admitted in pediatrics ICU, 13.91% patients admitted in neonatal ward (NW), and 1.39% patients admitted in outpatient department (OPD)

Unit	Percent	Frequency
A	22.10	1608
B	18.80	1368
C	18.75	1364
G	12.41	903
ICU	12.64	920
NW	13.91	1012
OPD	1.39	101
Total	100.0	7276

Table 4: *Place distribution of samples for meningitis patients at Pediatric Hospital from Summer 2017 to Spring 2019.*

Figure 3 explains the distribution of the sample items according to the hospital department.

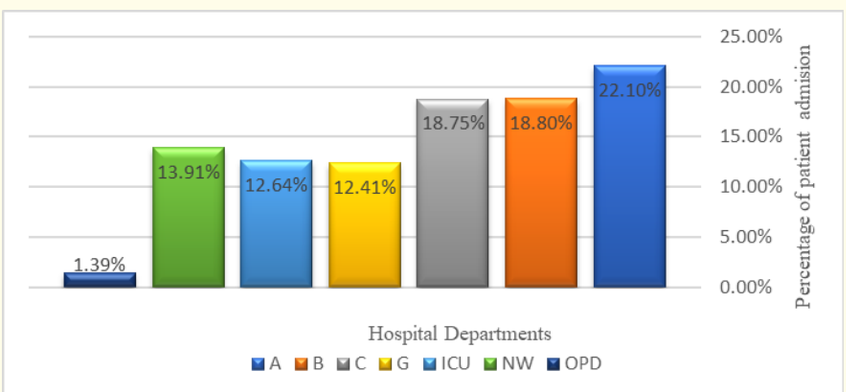

Figure 3: *Place distribution of samples for meningitis patients at pediatric hospital from summer 2017 to spring 2019.*

Organisms isolated from CSF cultures of patients of bacterial meningitis in Benghazi pediatric hospital from summer 2017 to spring 2019

The most commonly isolated pathogen was Gram negative bacilli 30 (20.5%), followed by *Haemophilus influenzae* 20 (14%), *Streptococcus pneumonia* 18 (12%), *Neisseria meningitides* and *E. coli* 16 (11%) equally, *Pseudomonas* spp 14 (9.5%), *Staph albus and Staph epidermidis* 10 (7%) equally, while the lowest was *Staph aureus and Klebsiella* spp 6 (4%) equally as shown in table 5 and figure 4.

Bacterial growth	Frequency	Percent
Escherichia coli (E. coli)	16	11%
Gram negative bacilli	30	20.5%
Klebsiella spp.	6	4%
Pseudomonas spp	14	9.5%
Staphylococcus albus	10	7%
Staphylococcus aureus	6	4%
Staphylococcus epidermidis	10	7%
Neisseria meningitidis	16	11%
Haemophilus influenzae	20	14%
Streptococcus pneumoniae	18	12%

Table 5: *Organisms isolate from CSF cultures of patients of bacterial meningitis in Benghazi Pediatric Hospital from Summer 2017 to Spring 2019.*

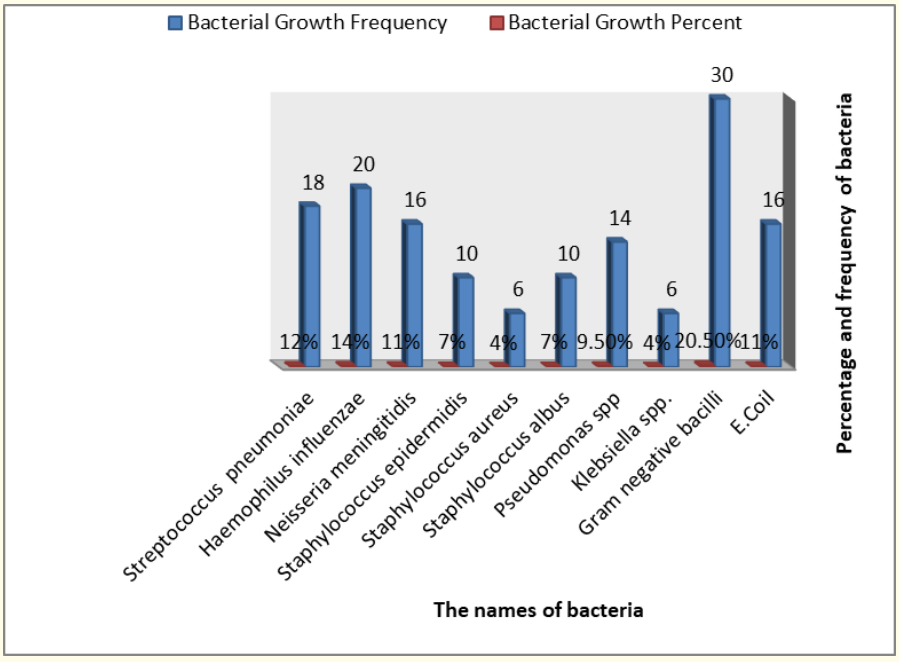

Figure 4: *Organisms isolated from CSF cultures of patients of bacterial meningitis in Benghazi pediatric hospital from summer 2017 to spring 2019.*

Seasonal variations in the bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019

Table 6 and figure 5 demonstrate that the majority of cases, 1218 (16.74%), were isolated in Summer 2018, followed by 1116 (15.34%) cases in Spring 2018 and 1017 (13.98%) in Autumn 2018, while the lowest incidence, 334 (4.59%), was observed in Summer 2017.

Seasons of the year	Frequency	Percent
Summer 2017	334	4.59
Autumn 2017	740	10.17
Winter 2018	876	12.04
Spring 2018	1116	15.34
Summer 2018	1218	16.74
Autumn 2018	1017	13.98
Winter 2019	1087	14.94
Spring 2019	888	12.20
Total	7276	100

Table 6: *Seasonal variations in the bacteria isolated from CSF at Benghazi Pediatric hospital from summer 2017 to spring 2019.*

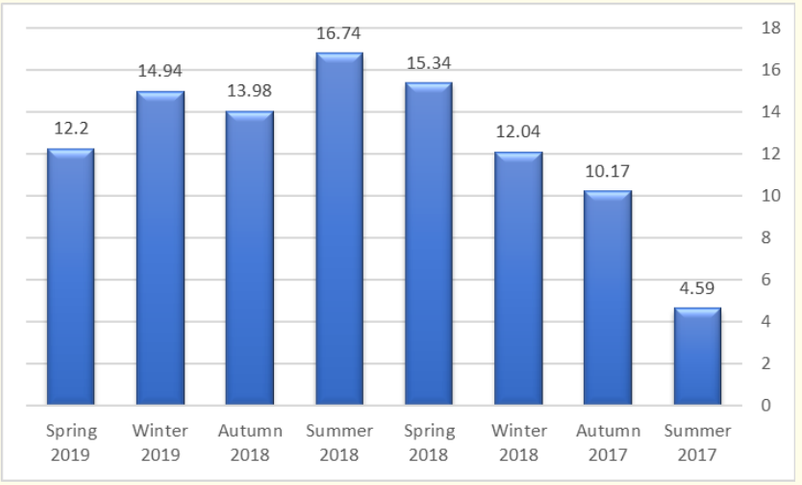

Figure 5: *Seasonal variations in the bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019.*

Susceptibility patterns of different bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019

Uniform antibiogram was used during the study period for all specimens; A-Ampicillin, Co-Cotrimoxazole, AMC-Augmentin, G-Gentamicin, VA-Vancomycin, FD-Fusidic acid, AK-Amikacin, CAR-Carbapenem, E-Erythromycin, CRL-Clarithromycin, Ox-Oxacillin, SXT-Sulfamethoxazole, IMP-Imipenem, AML-Amoxicillin, P-Penicillin G, CN- Cloxacillin, NA-Nalidixic acid, PIP-Piperacillin, CT-Colistin, CIP-Ciprofloxacin, CH-Chloramphenicol, R-Rifampicin, FOX-Cefotaxime, CFX-Ceftriaxone, T-Tetracycline, and CL-Clindamycin were the antibiotics that demonstrated *in-vitro* activity regularly (consistently?) against all cultured organisms. The isolated bacteria had the highest susceptibility to Ciprofloxacin 86 (58.9%), followed by Augmentin 53 (36.3%) and Ceftriaxone 48 (32.9%). The highest resistance was recorded towards Ampicillin 34 (23.3%), Sulfamethoxazole 32(21.9%), and Colistin 26 (17.8%) which is shown in table 7 and figure 6.

Type	CH	CIP	CT	SXT	OX	CRL	E	CAR	AK	FD	VA	G	AMC
R	15 10.3%	14 9.6%	26 17.8%	32 21.9%	6 4.11%	16 11%	13 8.9%	18 12.33%	4 2.74%	13 8.9%	12 8.22%	8 5.5%	28 19.2%
+	2 1.4%	4 2.74%	4 2.74%	3 2.1%	1 0.7%	2 1.4%	18 12.33%	2 1.4%	2 6%	3 2.1%	4 2.74%	3 2.1%	19 13%
++	1 0.7%	8 5.5%	18 12.33%	7 4.8%	1 0.7%	1 0.7%	2 1.4%	1 0.7%	2 6%	0 0%	2 1.4%	3 2.1%	2 1.4%
+++	9 6.2%	86 58.9%	41 28.1%	40 27.4%	14 9.6%	4 2.74%	36 24.7%	2 1.4%	1 0.7%	0 0%	18 12.33%	0 0%	53 36.3%

Co	A	CL	P	CFX	FOX	AML	R	T	CN	PIP	IMP	NA
9 6.16%	34 23.3%	1 0.7%	22 15.1%	0 0%	8 5.5%	16 11%	0 0%	1 0.7%	11 7.5%	0 0%	0 0%	0 0%
7 4.79%	3 2.1%	0 0%	7 4.79%	0 0%	0 0%	3 2.1%	0 0%	0 0%	7 4.79%	0 0%	0 0%	0 0%
4 2.74%	5 3.42%	0 0%	4 2.74%	0 0%	1 0.7%	10 6.9%	0 0%	0 0%	4 2.74%	0 0%	4 2.74%	0 0%
18 12.33%	12 8.22%	16 11%	18 12.33%	48 32.9%	35 24%	32 0.7%	30 20.6%	17 11.64%	22 15.1%	12 0%	10 6.9%	10 6.9%

Table 7: *Susceptibility patterns of different bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019.*

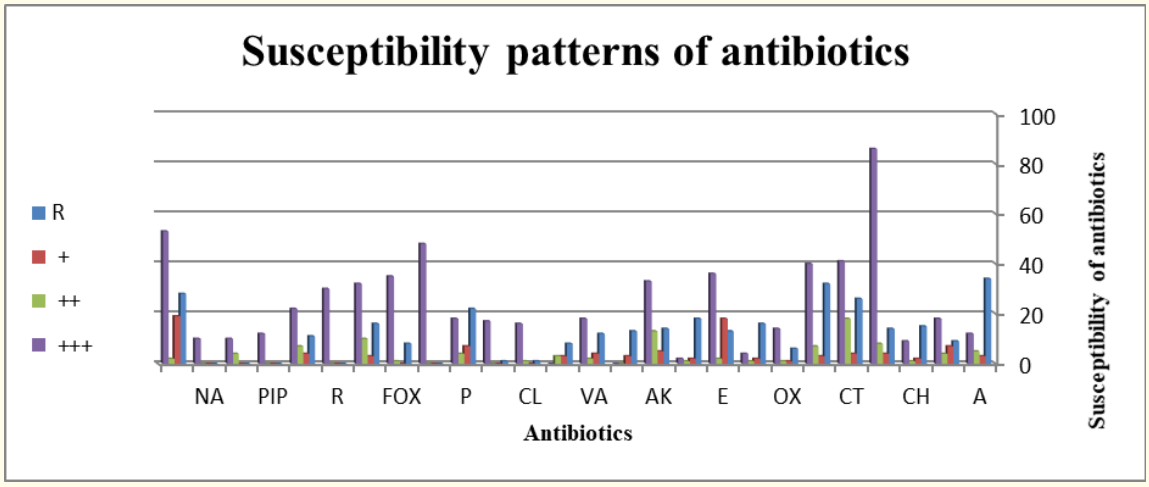

Figure 6: *Susceptibility patterns of different bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019.*

Susceptibility patterns of *Streptococcus pneumoniae* bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019

Streptococcus pneumoniae bacterial isolates were highly susceptible to Ciprofloxacin, Vancomycin, Ceftriaxone, and Augmentin and highly resistant towards Sulfamethoxazole and Penicillin G as depicted in figure 7.

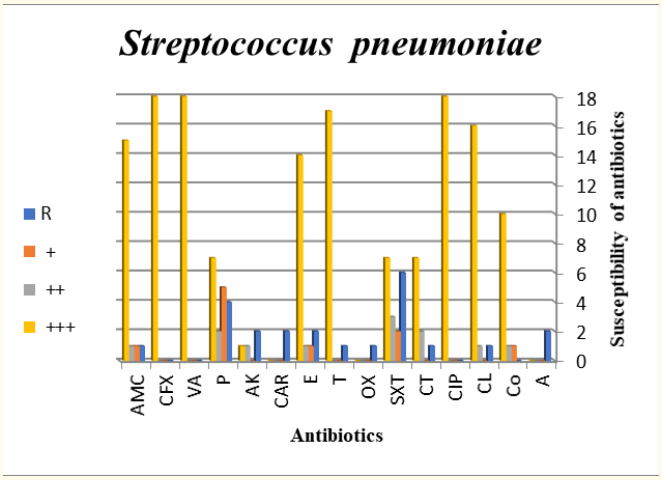

Figure 7: *Antimicrobial susceptibility pattern of Streptococcus pneumoniae on disc diffusion with MIC.*

Susceptibility patterns of *Escherichia coli* bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019

Escherichia coli bacterial isolates were highly susceptible to Ciprofloxacin and highly resistant towards Amikacin as depicted in figure 8.

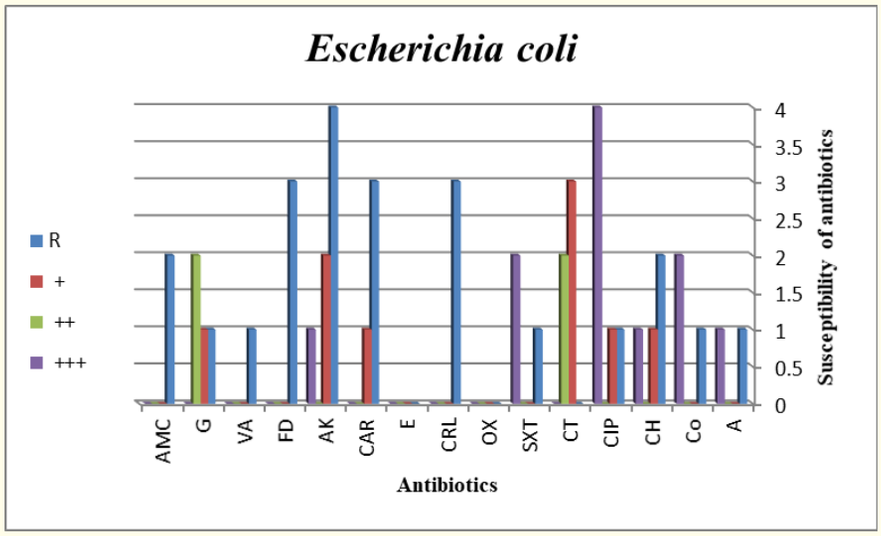

Figure 8: *Antimicrobial susceptibility pattern of Escherichia coli on disc diffusion with MIC.*

Susceptibility patterns of *Staphylococcus epidermidis* bacteria isolated from CSF at Benghazi Pediatric hospital from summer 2017 to spring 2019

Staphylococcus epidermidis bacterial isolates were highly susceptible to Cotrimoxazole and Vancomycin and highly resistant towards Ampicillin, Fusidic acid, and Augmentin as depicted in figure 9.

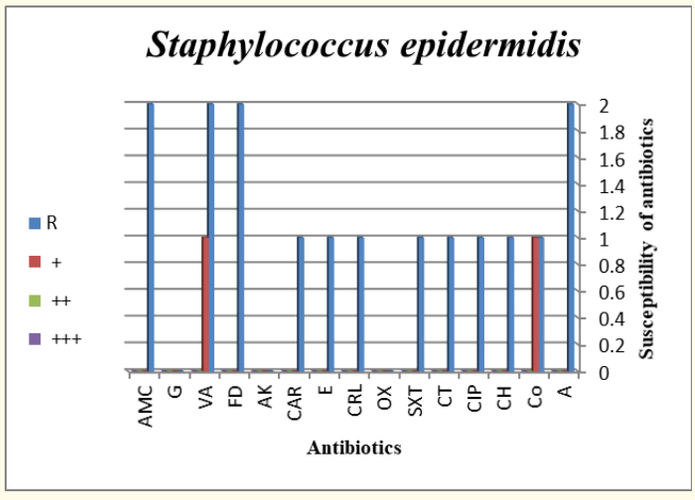

Figure 9: *Antimicrobial susceptibility pattern of Staphylococcus epidermidis on disc diffusion with MIC.*

Susceptibility patterns of *Staphylococcus albus* bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019

Staphylococcus albus bacterial isolates were highly susceptible to Cotrimoxazole and Erythromycin and highly resistant towards Vancomycin, Fusidic acid, and Augmentin as depicted in figure 10.

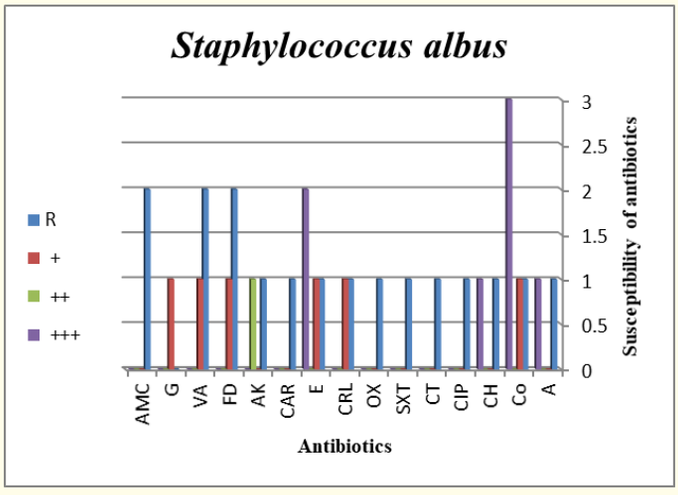

Figure 10: *Antimicrobial susceptibility pattern of Staphylococcus albus on disc diffusion with MIC.*

Susceptibility patterns of *Staphylococcus aureus* bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019

Staphylococcus aureus bacterial isolates were highly susceptible to Colistin, Ciprofloxacin and Chloramphenicol and highly resistant towards Vancomycin, Gentamicin, and Augmentin as depicted in figure 11.

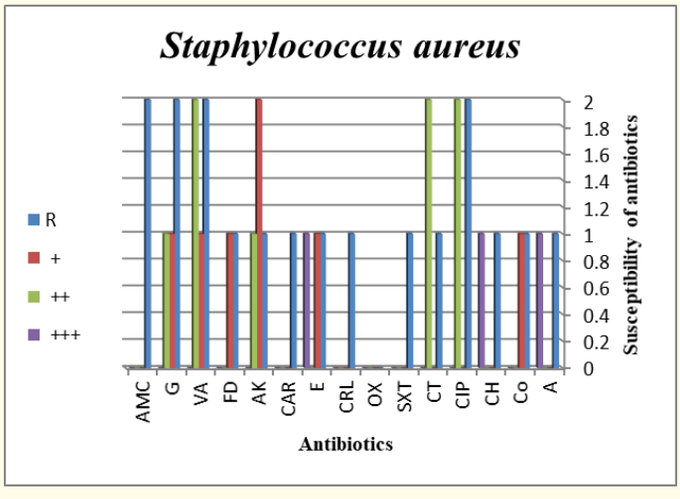

Figure 11: *Antimicrobial susceptibility pattern of Staphylococcus aureus on disc diffusion with MIC.*

Susceptibility patterns of *Klebsiella* spp. bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019

Klebsiella spp. bacterial isolates were highly susceptible to Ciprofloxacin and highly resistant towards Carbapenem, Clarithromycin, and Augmentin as depicted in figure 12.

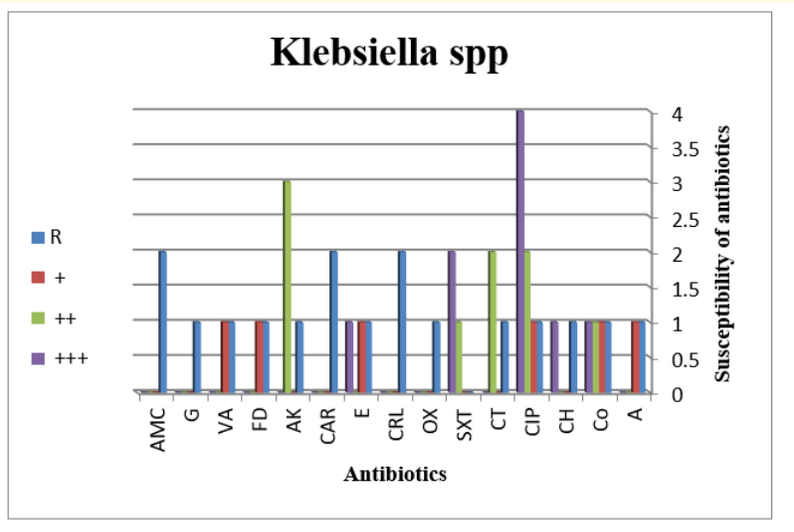

Figure 12: *Antimicrobial susceptibility pattern of Klebsiella spp. on disc diffusion with MIC.*

Susceptibility patterns of *Gram-negative bacilli* bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019

Gram negative bacilli bacterial isolates were highly susceptible to Amikacin and Ciprofloxacin and high resistant towards Augmentin followed by Colistin as shown in figure 13.

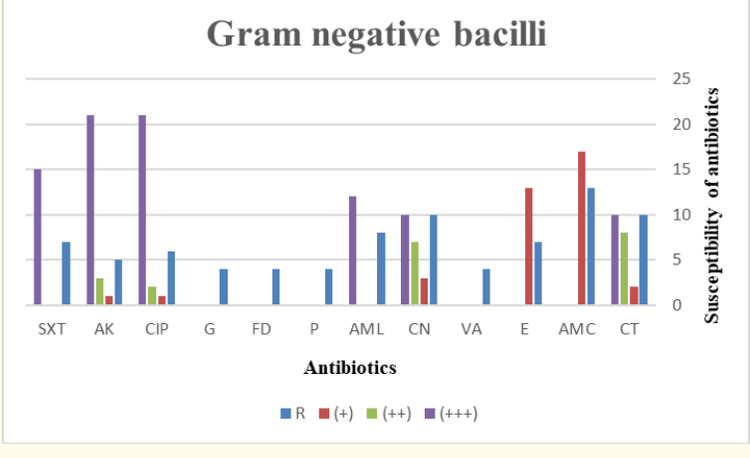

Figure 13: *Antimicrobial susceptibility pattern of Gram-negative bacilli on disc diffusion with MIC.*

Susceptibility patterns of *Pseudomonas aeruginosa* bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019

Pseudomonas aeruginosa bacterial isolates were highly susceptibility to Ciprofloxacin followed by Colistin, Augmentin, and Sulfamethoxazole and highly resistant towards Ampicillin and Cefotaxime as depicted in figure 14.

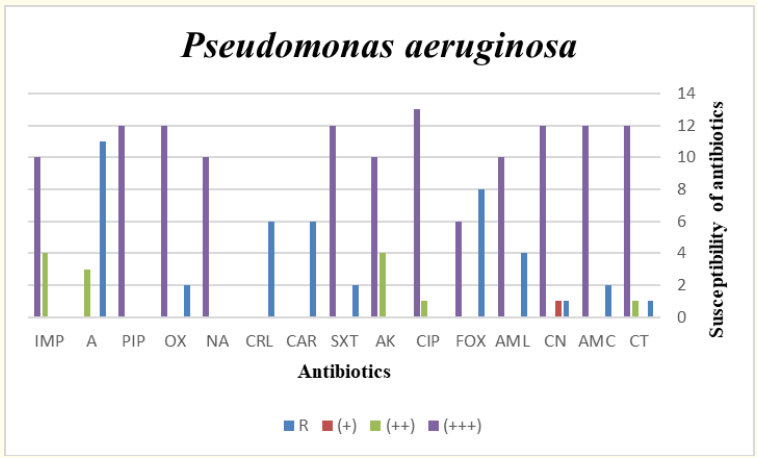

Figure 14: *Antimicrobial susceptibility pattern of Pseudomonas aeruginosa on disc diffusion with MIC.*

Susceptibility patterns of *Neisseria meningitidis* bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019

Neisseria meningitidis bacterial isolates were highly susceptible Cefotaxime, Ceftriaxone, Rifampicin, and Ciprofloxacin and highly resistant towards Sulfamethoxazole as depicted in figure 15.

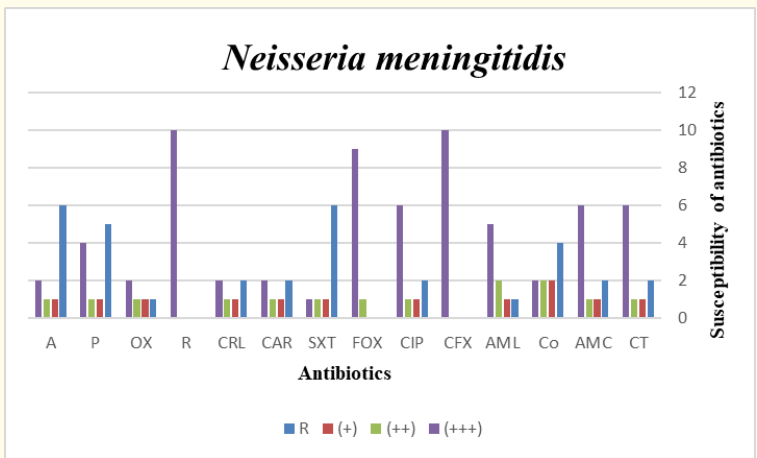

Figure 15: *Antimicrobial susceptibility pattern of Neisseria meningitidis on disc diffusion with MIC.*

Susceptibility patterns of *Haemophilus influenzae* bacteria isolated from CSF at Benghazi pediatric hospital from summer 2017 to spring 2019

Haemophilus influenzae bacterial isolates were highly susceptible to Augmentin, Cefotaxime, Ceftriaxone, Rifampicin, and Ciprofloxacin and highly resistant towards Ampicillin, Penicillin G, Chloramphenicol, Sulfamethoxazole, and Colistin as depicted in figure 16.

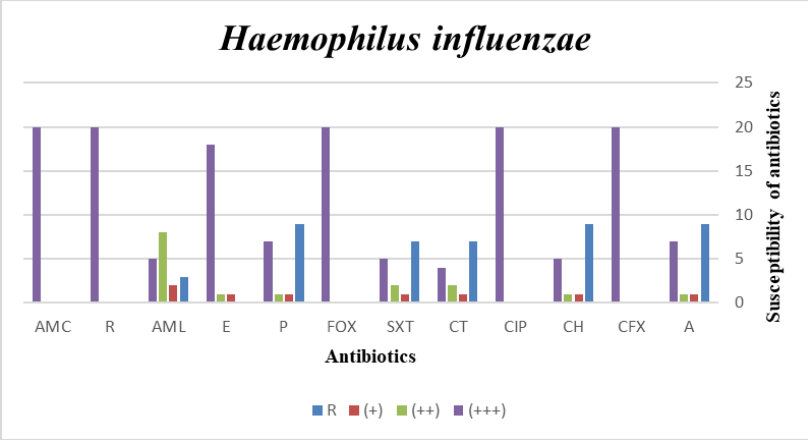

Figure 16: *Antimicrobial susceptibility pattern of Haemophilus influenzae on disc diffusion with MIC.*

Diagnostic tests for meningitis patients in Benghazi pediatric hospital from summer 2017 to spring 2019

WBC analysis for meningitis patients in Benghazi pediatric hospital from summer 2017 to spring 2019

Table 8 and figure 17 show that 7072 (97.2%) cases had normal WBC counts while 204 (2.80%) cases had elevated levels. Among the elevated levels, 154 (2.12%) cases had slightly raised levels indicating viral meningitis and 50 (0.68%) cases had highly raised levels indicating bacterial meningitis. In neonates, a CSF WBC cell count of > 15 cells/μL is consistent with meningeal inflammation, and bacterial meningitis should be a consideration. The CSF WBC count is typically greater in neonates with gram-negative meningitis than with meningitis caused by gram-positive organisms, but there is an overlap in many cases.

WBC	Frequency	Percent
Normal	7072	97.20%
Elevated	204	2.80%
Slightly raised (+)	154	2.12%
Highly raised (++)	50	0.68%
Total	7276	100

Table 8: *Distribution of WBC analysis for meningitis patients in Benghazi pediatric hospital from summer 2017 to spring 2019.*

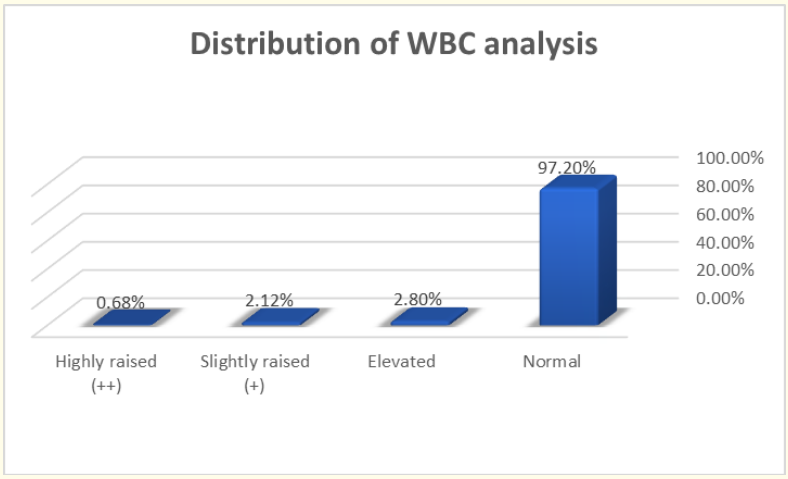

Figure 17: *WBC analysis for meningitis patients in Benghazi pediatric hospital from summer 2017 to spring 2019.*

Glucose analysis for meningitis patients in Benghazi pediatric hospital from summer 2017 to spring 2019

Table 9 and figure 18 shows that 7075 cases had normal while 201 cases had below normal glucose levels. Among those with below normal levels, 150 (2.06%) cases had slightly low levels indicating viral meningitis and 51 (0.7%) cases had low glucose levels, indicating towards bacterial meningitis. In bacterial meningitis, the CSF glucose level (reference range, 40-70 mg/dL) is less than 40 mg/dL in 60% of patients-and usually the levels are within the reference range or slightly low in viral meningitis.

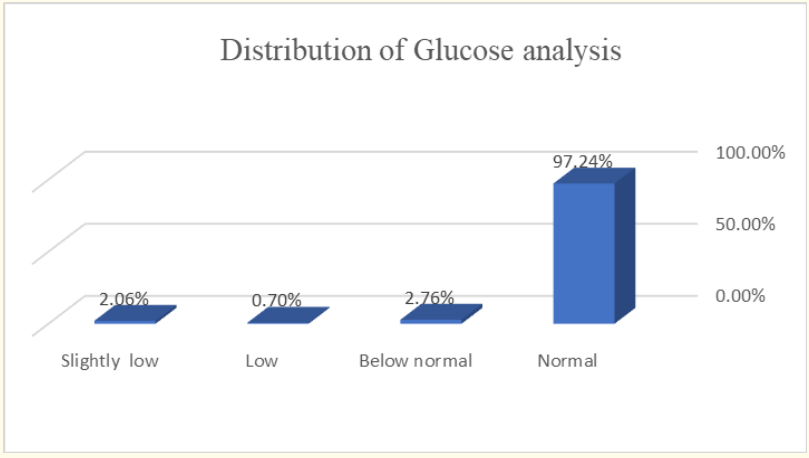

Figure 18: *Glucose analysis for meningitis patients in Benghazi pediatric hospital from summer 2017 to spring 2019.*

Glucose	Frequency	Percent
Normal	7075	97.24%
Below normal	201	2.76%
Low (--)	51	0.7%
Slightly low (-)	150	2.06%
Total	7276	100

Table 9: *Distribution of glucose analysis for meningitis patients in Benghazi pediatric hospital from summer 2017 to spring 2019.*

Protein analysis for meningitis patients in Benghazi pediatric hospital from summer 2017 to spring 2019

Table 10 and figure 19 shows that 7081 (97.32%) cases had normal while 195 (2.68%) cases had elevated protein levels. Among those with elevated levels, 150 (2.06%) cases had slightly elevated levels indicating viral meningitis, whereas 45 (0.62%) cases had highly elevated levels indicating bacterial meningitis. The CSF protein level (reference range, 20 - 50 mg/dL) is elevated in bacterial meningitis and in viral meningitis, the levels are usually normal to slightly elevated.

Protein	Frequency	Percent
Normal	7081	97.32%
Elevated	195	2.68%
Highly Elevated (++)	45	0.62%
Slightly Elevated (+)	150	2.06%
Total	7276	100

Table 10: *Distribution of protein analysis for meningitis patients in Benghazi Pediatric Hospital from Summer 2017 to Spring 2019.*

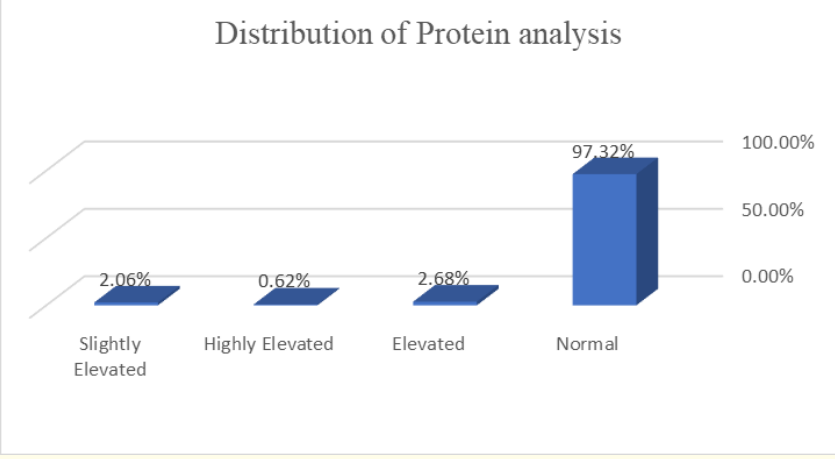

Figure 19: *Protein analysis for meningitis patients in Benghazi pediatric hospital from summer 2017 to spring 2019.*

Mortality rate for meningitis patients in Benghazi pediatric hospital from summer 2017 to spring 2019

Table 11 and figure 20 show that 90% of children with bacterial meningitis recovered completely with no long-term complications. Usually, children begin to improve within 24 to 36 hours after starting antibiotics. However, 10% of patients with meningitis experienced brain damage which lead to long-term sequelae such as deafness, developmental delays, learning disabilities, spastic or paralyzed muscles, and seizures. The Libyan Ministry of Health offers free vaccinations against meningitis to children from birth till they enter school at the age of …….

Mortality rate	Frequency	Percent
Death	0	0%
Recovered or treated patient	540	90%
Sequelae/ complications	60	10%
Deafness	12	2%
Developmental delay	12	2%
Learning disabilities	12	2%
Spastic or paralyzed muscles	12	2%
Seizures	12	2%
Total	600	100%

Table 11: *Mortality rate for meningitis patients in Benghazi pediatric hospital from summer 2017 to spring 2019.*

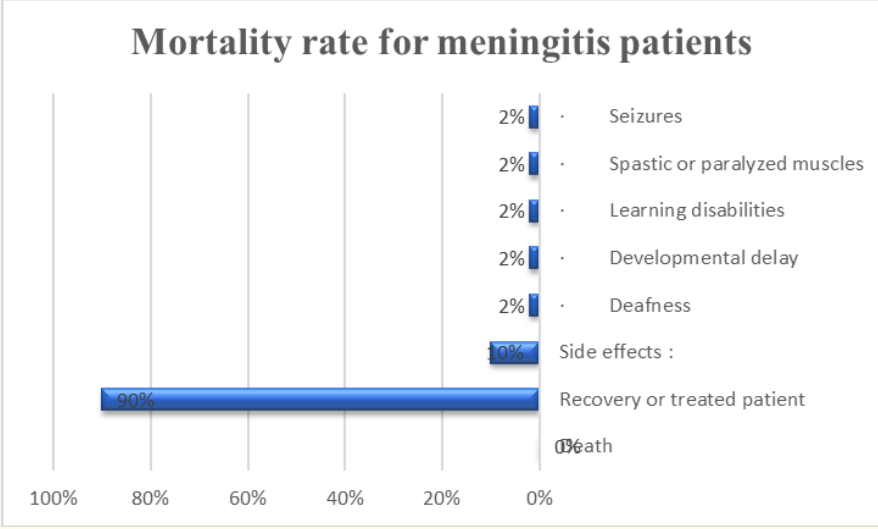

Figure 20: *Mortality rate for meningitis patients in Benghazi pediatric hospital from summer 2017 to spring 2019 (may change recovery to recovered).*

In our study, 7276 cerebrospinal fluids (CSF) samples were collected from patients suspected of meningitis in Benghazi Pediatric Hospital from Summer 2017 to Spring 2019 out of which there were 600 positive meningitis patients. 146 (2%) patients who tested positive had bacterial meningitis while 454 (6.24%) had viral meningitis.

Blood cultures are needed to complement the CSF culture as blood cultures are positive in 50% patients with meningitis due to *H. influenzae*, *S. pneumoniae*, or *N. meningitidis*. As many as 50% patients with pneumococcal meningitis also have evidence of pneumonia on an initial chest radiography. In additon, serum procalcitonin (PCT) levels can be used as a guide to distinguish between bacterial and aseptic meningitis in children as elevated serum PCT levels predict bacterial meningitis. The CSF bacterial cultures yield the bacterial cause in 70 - 85% of cases. The yield diminishes by 20% in patients who have received antimicrobial therapy. There is no treatment for viral meningitis, and in Benghazi Pediatrics Hospital the indications for hospitalization include appearance or signs of encephalitis (e.g. altered or depressed mental state, focal neurologic abnormalities, seizures), need for empiric antimicrobial treatment, need for intravenous hydration or aggressive pain control, immunocompromised host, and age younger than one year[8]. Supportive care for children with viral meningitis may include staying in a quiet and dimly lit room, Acetaminophen and/or Ibuprofen for headache, pain, and fever (Aspirin should be avoided because of its association with Reye syndrome), and intravenous fluid therapy if poor oral intake and/or prolonged emesis have resulted in hypovolemia. Careful attention to fluid balance is an important aspect of supportive care. The need for fluid repletion must be balanced against the risk of inappropriate secretion of antidiuretic hormone[8].

Discussion

In this clinical prospective longitudinal study, seven thousand and two hundred seventy-six (7276) cases with suspected meningitis were examined using culture in a microbiology and a hematology laboratory for CSF fluid. Gender distribution showed that 4039 (55.5%) participants were males and 3237 (44.5%) participants were females. Among 7276 cerebrospinal fluid (CSF) samples collected from patients suspected of meningitis in Benghazi Pediatric Hospital, 146 (2%) were positive for bacterial meningitis and 454 (6.24%) were positive for viral meningitis. The common isolated pathogens were Gram negative bacilli 30 (20.5%), followed by *Haemophilus influenzae* 20 (14%), *Streptococcus pneumonia* 18 (12%), *Neisseria meningitides* and *E. coli* 16 (11%) equally, *Pseudomonas* spp 14 (9.5%), *Staph albus* and *Staph epidermidis* 10 (7%) equally, *Klebsiella* spp and *Staph aureus* 6 (4%) equally, which is in accordance with the study conducted by Ghotaslou., *et al.* from the Iran, published in 2012 [9]. 50% of blood cultures were positive in meningitis caused by *H. influenzae*, *S. pneumoniae*, or *N. meningitidis*. As many as 50% of patients with pneumococcal meningitis also had evidence of pneumonia on an initial chest radiography. The frequency of viral meningitis increases slightly during the summer months due to larger exposure to viruses [10]. Despite advances in management, bacterial meningitis remains a life-threatening infection with high rates of morbidity and mortality [11]. Early clinical suspicion and implementation of appropriate antimicrobial medical aid are essential in reducing adverse outcomes. A CSF culture is diagnostic for bacterial meningitis, and bacterial isolation is vital for antimicrobial status testing and molecular medicine [12-14]. Molecular techniques for each respective type of microorganism and infective agent are quickly turning into the gold standard, however, these methods are simply not on the market in African nations because of their high costs. Therefore, for our comparisons we used a positive result by any of the two check methodologies i.e. by Gram's staining method and CSF culture. Of the 7276 CSF samples, 146 (2%) demonstrated vital growth during this study. In similar studies conducted in Nepal, significant growths of varied isolates were detected in addition by Shah of Iran., *et al.* (3.7%) in 2001 [15] and Ansari., *et al.* (4.4%) in 2011 [16]. Proportionately, a high rate of bacterial growth (17.7%) was detected by Wu dialect., *et al.* in 2013 [17]. The speed of positive yield of microorganism depends on variety of factors, for example, the time of lumber puncture, the probable number of bacteria in Gram's stained preparation of CSF, and the medicinal drug aid before lumber puncture [18] as well. During this study, among the registered cases, the children of age group 2-10 years old were found to be the most vulnerable age group of children and accounted for 40% of total positive cases. This was followed by children 2 months to 2 years old which accounted for 30% of total positive cases and the children from 2 to 10 years old which accounted for 20% of positive cases. Similarly, the high rate of meningitis (32.1%) was also detected in children 6 - 12 months old from Asian nations by Joshi Batajoo

[19]. The higher rate of infectious diseases in early age children could also be caused by an underdeveloped immune system. A Medical specialty profile (Gram staining and culture result) of CSF facilitates the selection of an antibiotic medical aid [20]. CSF culture sensitivities usually vary between seventy to ninety yuletides [12-14] with variation due to inclusion criteria, patient characteristics, laboratory practices, and the spectrum of pathogenic microorganisms [17]. Gram staining, a mainstay of bacterial meningitis diagnosis, is widely available, affordable and yields rapid results [11]. Our study also identified one case of meningitis associated with Streptococcus species which could have been due to an underlying disease, however, we couldn't evaluate the predisposing factors for the same case. Once there is suspicion of infectious disease, there should to be no delay in beginning empiric antibiotics for which information of common pathogens and their antibiotic susceptibilities is required. During this study, the bacteria isolated were highly susceptible to Ciprofloxacin 86 (58.9%), followed by Augmentin 53 (36.3%), Ceftriaxone 48 (32.9%), Cotrimoxazole 18 (12.32%), Ampicillin 12 (8.22%), and Chloramphenicol 9 (6.2%). The highest resistance was recorded towards Ampicillin 34 (23.3%) followed by Sulfamethoxazole 32 (21.9%), Chloramphenicol 15 (10.3%), and Cotrimoxazole 9 (6.2%). The results of our study corroborate with Mastro., *et al.* (1991) a United Nations agency that reported only 2.8% strains resistant to chloramphenicol [21]. Ampicillin and Cotrimoxazole were the least effective antibiotics against the isolates. In contrast, the higher resistance rate (64.1%) to Cotrimoxazole was reported by Saha., *et al.* in 1997 from Nepal [22]. The higher rate of Cotrimoxazole resistance was presumably correlated with the wide use of this antibiotic within those communities due to its dose convenience, effectiveness, easy accessibility, and prescribing trends in treating suspected cases of infectious respiratory disorders. In our study, 90% of children with bacterial meningitis recovered completely with no long-term complications whereas, 10% of patients suffered some form of brain damage resulting in long-term complications, such as deafness, developmental delay or learning disabilities, spastic or paralyzed muscles, and seizures. These results are contradictory to those of a study by Al-Harthi., *et al*. from Saudi Arabia who detected a higher mortality rate of 48% [23]. A medical diagnosis of meningitis needs to be differentiated between viral, tuberculous, and acute bacterial meningitis. For preventing the ~~of~~ transmission of diseases, vaccination against the organisms, and chemoprophylaxis is recommended. Immunization is considered as the most effective method of protection from causative microorganisms of meningitis in children. Universal immunization with the conjugated vaccines has reduced the invasive diseases caused by *H. influenzae* blood type by over 99% in developed countries [24]. The prices and implementation of those vaccines in developing countries creates intimidating problems. The Libyan Ministry of Health offers free vaccinations against meningitis to children from birth till they enter school (age?). In our study, among the culture positive organisms, *Haemophilus influenzae* 20 (14%) was reported as the number one causative agent followed by Gram negative bacilli 30 (20.5%), *Streptococcus pneumonia* 18 (12%), *E. coli* and *Neisseria meningitides* 16 (11%). Out of the eight *H. influenzae* positive cases, five were detected in children below two years of age. Despite the *H. influenzae* blood type (Hib) vaccination, it has been found as the number one reason for infectious disease. The vaccination coverage and *H. influenzae* capsular sorts could be another reason. However, the higher rate in some ethnic families, and the observation that siblings of patients with meningitis will have deficient protein synthesis against *H. influenzae*, indicate that genetic predisposition to infection most likely exists [25]. The danger of acquiring a secondary bacterial infection (due to) haemophilus or a meningococcal disease is highly increased once exposed to the primary infection within the home [26]. Although, blood stream related infection is a leading reason behind infectious disease in neonates, this organism has also been recognized with increasing frequency as a considerable cause of meningitis in later age groups [27].

Conclusions and Recommendation

Gram negative bacilli 30 (20.5%), followed by *Haemophilus influenzae* 20 (14%), *Streptococcus pneumonia* 18 (12%), *Neisseria meningitides* and *E. coli* 16 (11%) equally, *Pseudomonas* spp 14 (9.5%), *Staph albus* and *Staph epidermidis* 10 (7%) equally, and *Klebsiella* spp and *Staph aureus* 6 (4%) equally, remained the major etiological agents of Community Acquired Acute Bacterial Meningitis (CAABM) in children in this study. Meningitis causing bacteria were resistant to Ampicillin 34 (23.3%) followed by Sulfamethoxazole 32 (21.9%), Augmentin 28 (19.2%), and Colistin 26 (17.8%). An additional study should focus on features of vaccines to reduce the disease problem. The infectious diseases are abundant in children up to fifteen years of age as shown in this study. A transmission of Gram positive and Gram negative organisms was also documented. Therefore, we suggest educating the general public to enhance awareness on adequate protec-

tion and appropriate drug management. In our study, only 14% of infections resulted from *H. influenzae*, confirming consistent decrease in incidence since the introduction of effective conjugated vaccine (requiring three primary doses and one booster dose), that currently covers 100% of Libyan children, as in developing countries [28,29].

Conclusion

In conclusion, the antibiotic susceptibility patterns among causative bacteria in childhood meningitis will serve as a guide for empiric antibiotic treatment and vaccine development. This knowledge additionally represents a benchmark against which the impact of recent conjugate vaccines can be gauged.

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