

# Meningitis In Sulaimani Pediatric Teaching Hospital: A Retrospective Study

Seenaa Muhammed Ali <sup>1</sup>, Heersh Hma Raof Saeed <sup>2</sup>, Khalid Rashid Suliman <sup>3</sup>

<sup>1,3</sup> Department of community health, Technical college of health, Sulaimani polytechnic University. Sulaimani/Iraq.

<sup>2</sup> Department of pediatrics, Faculty of medical science, Sulaimani University. Sulaimani/Iraq

Date Submitted:24/1/2017

Date Accepted:27/3/2017

## Address for Correspondence:

Seenaa Muhammed Ali · Department  
of community health, Technical  
college of health, Sulaimani  
polytechnic University.  
Sulaimani/Iraq

## Abstract

**Background:** Meningitis in children is one of the life threatening condition in pediatric age group, which needs proper and early diagnosis in the emergency department. Meningitis morbidity and mortality depend on causative agent, time of diagnosis, proper and sufficient duration of therapy in the hospital. For diagnosis, many parameters can be used from history, physical examination and laboratory investigation, which needs sophisticated laboratory to perform.

**Objective:** To analyze CSF findings in children admitted to hospital as meningitis (bacterial and non-bacterial). Also, assess frequency and percentage of the bacterial species isolated from positive CSF culture and determine the resistance patterns of the different bacterial pathogens.

**Method:** A retrospective study carried out in Sulaimania, Iraq/pediatric teaching hospital from January to December 2014. lumbar puncture done in 96 cases aged between 29 days to 15 years that have been diagnosed as meningitis CSF parameters; WBC total count, Sugar and protein level were examined, also culture done for all cases with CSF leukocytosis .

**Results:** According to CSF findings and clinical diagnosis, 51% (49cases) considered bacterial while 49% (47 cases) considered non bacterial meningitis. Deaths recorded only among Bacterial meningitis patients with a percentage of 6.1%. Results of CSF culture determined a 24 % (22 cases) as positive for bacterial growth. *Streptococcal pneumonia*, was on the top of the isolated bacteria with a high resistance against penicillin and Azithromycin.

**Conclusion:** Bacterial meningitis are still occupying large percentage of cases admitted to hospital, and if un-diagnosed promptly will have a high mortality. High index of suspicion for bacterial meningitis is recommended.

**Key words:** meningitis, bacterial, non bacterial, CSF, CSF culture

## INTRODUCTION

Infection of the central nervous system (CNS) is one of the causes of fever in pediatrics' age group. Many microorganisms can cause infection including bacterial, viral, and fungal.<sup>(1)</sup> The presence of microorganisms in normally sterile body fluid specimens may be representative of life threatening infections.<sup>(2)</sup> Regardless of etiology, most patients with CNS infection have similar clinical manifestations. Common symptoms include headache, nausea, vomiting, anorexia, restlessness, altered state of consciousness, and irritability; most of these symptoms

are nonspecific. Common signs of CNS infection, in addition to fever, include photophobia, neck pain and rigidity, bulging fontanelle in children below 18 months, obtundation, stupor, coma, seizures, and focal neurologic deficits.<sup>(1)</sup>

Differentiating bacterial from nonbacterial meningitis is very important in deciding treatment. Bacterial meningitis is a life-threatening neurological condition and needs prompt parenteral antibiotics, compared to viral and aseptic meningitis, which carries relatively better outcome.<sup>(3)</sup>

Acute bacterial meningitis is a major cause of death and disability worldwide. It affects over one million people yearly, with a higher incidence among developing countries and in specific geographic areas.<sup>(4)</sup>

Bacterial meningitis are considered as one of the most serious infection in infant and children, which causes numerous complications and high mortality if not diagnosed and treated timely. Therefore, early diagnosis, early implementation and appropriate antimicrobial therapy are necessary to avoid further complication.<sup>(5)</sup> Untreated bacterial meningitis is highly fatal, leaving serious neurological sequelae in survivors and crippling children in their lifetime.<sup>(6)</sup>

Analysis of the CSF is critical to the diagnosis of meningitis and the differentiation of bacteria from other etiologies. A lumbar puncture should be performed on any child in whom the diagnosis of meningitis is suspected, unless specific contraindications to the LP are present.<sup>(7)</sup>

Other indications for analyzing CSF include diagnosing GuillainBarré syndrome, other demyelinating processes, diagnosing and treating pseudo tumor cerebri.<sup>(8)</sup>

The classic CSF abnormalities in bacterial meningitis are a polymorphonuclear leukocytosis, decreased glucose concentration, and increased protein concentration. In viral meningitis, the classic CSF abnormalities are a lymphocytic pleocytosis, a normal glucose concentration (except in Mump encephalitis which may cause low CSF sugar), and a normal or slightly elevated protein concentration.<sup>(9)</sup>

A positive bacterial culture from CSF specimens is of great use to unequivocally diagnose bacterial meningitis and to identify the etiological agent.<sup>(10-11)</sup> Administration of antibiotics to children before the performance of diagnostic lumbar punctures increases the number of false-negative cerebro-spinal fluid bacterial culture results.<sup>(12,13)</sup> In recent years, a main changes have been observed in the epidemiology of acute bacterial meningitis when the effectiveness of treatment is limited due to increasing the multi-resistant bacterial strains.<sup>(14)</sup> Also the occurrence and etiologies of bacterial meningitis vary in different geographic regions.<sup>(15)</sup>

The aim of this study is to assess the role of CSF analysis in the diagnosis of meningitis cases (bacterial and non-bacterial). Also list the bacterial pathogens which isolated from our children and study the resistance pattern of these bacteria against different conventional antibiotics.

## PATIENTS AND METHODS

A retrospective study done in Sulaimani pediatric teaching hospital from 1<sup>st</sup> January to 31<sup>st</sup> December 2014. The Sulaimani pediatric teaching hospital is a 340 bed hospital located in Sulaimani city which is the center of Sulaimani Governorate in north of Iraq.

Children aged 29 days to 15 years who admitted to the hospital and diagnosed as meningitis were enrolled in this study. Exclusion criteria were children with papilledema and children who were cardiovascular unstable at time of admission. For all suspected meningitis cases, lumbar puncture done for cases below 18 months, and after fundoscopy for children older than 18 months in whom fontanels are closed. CSF samples were immediately sent to the hospital central laboratory. Laboratory tests included; CSF white blood cells count, glucose and protein levels. All the CSF specimens with leukocytosis were cultured on blood Agar, chocolate agar and MacConkey Agar. Automated analysis system VITEK 2 (bioMerieux) was used to identify the isolated bacteria. The routine method of disk diffusion test was used to examine the resistance of the isolates against nine different conventional antibiotics; Ceftriaxone (30µg/ml), Cefotaxime (30 µg/ml), Ceftazidime (30 µg/ml), Ciprofloxacin (5 µg/ml), Trimethoprim (25 µg/ml), Ampicillin, (10 µg/ml) Vancomycin (30 µg/ml), Azithromycin (15 µg/ml), and Penicillin (10 µg/ml).

## RESULTS

Out of 96 cases were enrolled in this study, 47 (49%) of cases diagnosed as non-bacterial meningitis, and 49 (51%) of cases diagnosed as bacterial meningitis. Among the bacterial meningitis patients, three deaths (6.1%) were recorded, and all these deaths occurred in children under 2 years old.

Table 1 shows that 65 (68%) of cases were male, while 31 (32%) of cases were female in the ratio of (2:1). The percentage of male cases which diagnosed as non-bacterial were 49.2% (32), and 50.8% (33) of them diagnosed as bacterial meningitis; while 48.4% (15) of female cases were diagnosed as non-bacterial meningitis and 51.6% (16) of them diagnosed as bacterial meningitis.

**Table 1: Sex distribution of Meningitis cases**

| Gender | Non bacterial meningitis |             | Bacterial meningitis |             |
|--------|--------------------------|-------------|----------------------|-------------|
|        | Number of cases          | percentage% | Number of cases      | percentage% |
| Female | 15                       | 48.4        | 16                   | 51.6        |
| Male   | 32                       | 49.2        | 33                   | 50.8        |

Table 2 shows that in non-bacterial meningitis 74.5% of the cases have a WBC count between 100-1000 and just 8.5% of cases with a WBC count more than 1000 cell/mm<sup>3</sup>. In bacterial meningitis only 2% has a WBC

count less than 100 cell/mm<sup>3</sup>, and 61.2% of cases have a WBC count more than 1000 cell/mm<sup>3</sup>. Patients with bacterial meningitis had a predominantly neutrophilic CSF in 89.1% of the cases. On the other hand, patients with nonbacterial meningitis had a predominantly lymphocytic CSF in 89.4% of the cases.

Percentage of CSF glucose was normal in 91.5% of non-bacterial meningitis patients, while in 81.6% of bacterial meningitis was at a low ratio.

CSF protein in non-bacterial meningitis result showed that 41.3% of the cases have slight elevation of CSF protein and 32.6% of the cases have moderate elevation of CSF protein while in bacterial meningitis 14% of the cases have normal CSF protein and 42% of the cases have marked elevation of CSF protein (Table 2).

**Table (2): CSF parameters in bacterial and non-bacterial meningitis**

| CSF parameter                              |                                   | Type of meningitis       |      |                      |      |
|--------------------------------------------|-----------------------------------|--------------------------|------|----------------------|------|
|                                            |                                   | Non-bacterial meningitis |      | Bacterial meningitis |      |
|                                            |                                   | Number                   | %    | Number               | %    |
| <b>WBC total count cell/mm<sup>3</sup></b> | less than 100                     | 8                        | 17   | 4                    | 8.5  |
|                                            | 100–1000                          | 35                       | 74.5 | 18                   | 36.7 |
|                                            | more than 1000                    | 1                        | 2    | 30                   | 61.2 |
| <b>CSF Neutrophil %</b>                    | More than 50%                     | 5                        | 10.6 | 44                   | 89.1 |
|                                            | Less than 50%                     | 42                       | 89.4 | 5                    | 10.9 |
| <b>CSF Sugar (mg/dL)</b>                   | Normal (more than 45)             | 43                       | 91.5 | 9                    | 18.4 |
|                                            | Low (less than 45)                | 4                        | 8.5  | 40                   | 81.6 |
| <b>CSF protein (mg/dL)</b>                 | Normal CSF protein (less than 45) | 7                        | 15.2 | 7                    | 14   |
|                                            | Slight elevation (45-75)          | 19                       | 41.3 | 8                    | 16   |
|                                            | Moderate elevation (75-100)       | 15                       | 32.6 | 14                   | 28   |
|                                            | Marked elevation (more than 100)  | 5                        | 10.9 | 21                   | 42   |

Regarding The CSF culture results, 22 from 49 cases of bacterial meningitis have positive CSF culture. The most predominant organisms were *Streptococcus pneumonia* with a percentage of (36.36 %). The prevalence of other bacterial isolates are listed in Table 3.

**Table (3): Number and percentage of the bacterial isolates**

| Microorganisms                 | No. isolates | Percentage |
|--------------------------------|--------------|------------|
| <i>Streptococcus pneumonia</i> | 8            | 36.36      |
| <i>Staphylococcus aureus</i>   | 3            | 13.63      |
| <i>Enterobacter species</i>    | 3            | 13.63      |
| <i>E. coli</i>                 | 2            | 9.09       |
| <i>Pseudomonas aeruginosa</i>  | 2            | 9.09       |
| <i>Streptococcus pyogenes</i>  | 1            | 4.54       |
| <i>Listeria monocytogns</i>    | 1            | 4.54       |
| <i>Enterococcus fuecium</i>    | 1            | 4.54       |
| <i>Kocuria virians</i>         | 1            | 4.54       |
| <b>Total</b>                   | <b>22</b>    |            |

The results of resistance pattern to the isolated bacteria (Table 4) showed that the eight isolates of *S. pneumoniae* had high resistance against penicillin and Azithromycin .Moreover, these isolates had intermediate resistance against Ceftazidime. In addition, the resistance of *E.coli* isolates against the third generation cephalosporins was considerable, also the two strains were resistant against Ampicillin.

Table (4): Percentage of antimicrobial resistance of bacterial pathogens isolated from CSF culture.

| Antibiotics   | <i>Streptococcus pneumoniae</i> | <i>Staphylococcus aureus</i> | <i>Enterobacter species</i> | <i>E.coli</i> | <i>Pseudomonas aeruginosa</i> | <i>Streptococcus pyogenes</i> | <i>Listeria monocytogenes</i> | <i>Enterococcus faecium</i> | <i>Kocuria virians</i> |
|---------------|---------------------------------|------------------------------|-----------------------------|---------------|-------------------------------|-------------------------------|-------------------------------|-----------------------------|------------------------|
| Ceftriaxone   | 12.5                            | -                            | -                           | 50            | 100                           | 0                             | 100                           | 100                         | 0                      |
| Cefotaxime    | -                               | -                            | 33.3                        | 50            | 100                           | -                             | -                             | 0                           | 0                      |
| Ceftazidime   | 37.5                            | -                            | 66.6                        | 100           | 100                           | 100                           | 0                             |                             |                        |
| Ciprofloxacin | 0                               | 33.3                         | 0                           | 50            | 0                             | 0                             | 100                           | 100                         | 100                    |
| Trimethoprim  | -                               | 33.3                         | 66.6                        | 50            | 50                            | -                             | 0                             | -                           | -                      |
| Ampicillin    | -                               | 33.3                         | 33.3                        | 100           | -                             | -                             | 100                           | -                           | -                      |
| Vancomycin    | -                               | 33.3                         | -                           | -             | -                             | 0                             | -                             | -                           | -                      |
| Azithromycin  | 50                              | 33.3                         | -                           | -             | -                             | 0                             | -                             | 100                         | 0                      |
| Penicillin    | 62.5                            | 33.3                         | -                           | -             | -                             | -                             | -                             | 100                         | 100                    |

## DISCUSSION

During the year 2014, (106) meningitis cases aged between 29 days and 15 years admitted to Sulaimani pediatric teaching hospital. Diagnosis of these cases depends upon history, physical examination (especially neurological examination), examination for signs of meningism, and positive CSF finding. After excluding cases of papilledema and unstable case we found 96 cases diagnosed as meningitis.

According to our study, 68% of cases were males and 32% of cases were females, with the ratio of male to female 2:1, this corresponds with studies carried out in Iran/Tehran metropolitan area with a ratio of 2:1,<sup>(16)</sup> and other studies showed also a male preponderance of 1.27:1, 1.2:1 and 1.07: respectively.<sup>(6,17,18)</sup> Factors underlying these sex differences are poorly understood, but a hypothetical model was developed which assumes increased susceptibility to infectious disease such as relative immune deficiency in a proportion of males.<sup>(19)</sup>

In this study, out of 96 cases (49%) were diagnosed as non-bacterial meningitis versus (51%) of cases diagnosed as bacterial meningitis, this little increase in percentage of bacterial meningitis incidences agrees with several reports written on childhood meningitis from almost every region of Saudi Arabia.<sup>(20,21,22)</sup> Another study done in Egypt (Rabab et al) shows that among 623 meningitis cases, bacterial meningitis represented 73.3%, compared to 26.7% non-bacterial meningitis of the studied population.<sup>(23)</sup>

While a higher percentage of non bacterial meningitis (87.34%) seen in another study done in Pittsburgh by Negrini et al who studied one hundred fifty-eight cases of meningitis.<sup>(24)</sup> High percentage of bacterial meningitis in some countries compared with viral meningitis in other countries is of multifactorial, but the most probable cause is a vaccination program “There are effective vaccines against the three major bacterial pathogens responsible for bacterial meningitis, *Streptococcus pneumonia*, *Haemophilus influenza*, and *Neisseria meningitis*”.<sup>(25)</sup> In our

country, service of meningitis vaccine is often not available, and also the low socioeconomic state is regarded as a risk factor for increasing bacterial infection.

This study revealed that non bacterial meningitis (74.5%) CSF leukocyte count was between 100 -1000 cell/mm<sup>3</sup>, this corresponds with other studies done in; Portugal , Egypt, South Korea, which showed that mean cell count in aseptic meningitis is 159 cell/mm<sup>3</sup>, 8.2×10/mm<sup>3</sup>, 8,306 cells/mm<sup>3</sup> respectively.<sup>(26,27,28)</sup> While bacterial meningitis (36.7 %) have a CSF leukocyte count between 100-1000 cell/mm<sup>3</sup> and 61.2% have a CSF leukocyte count of more than 1000 cell/mm<sup>3</sup>. Many other studies throughout the world showed same high CSF leukocytosis in bacterial meningitis, for example a study done in Egypt by Fouad et al,<sup>(23)</sup> and another study done at Children's Hospital of Pittsburgh by Negrini et al, showed significant CSF leukocytosis (mean CSF leukocyte count =3461.7 and median 1380).<sup>(24)</sup>

CSF glucose concentration is decreased in 81.6% of patients with bacterial meningitis and normal in 91.5% of the aseptic meningitis patients. CSF analysis showed that CSF protein concentration was markedly elevated in 42% of patients with bacterial meningitis and slight elevated in 41.3% of patients with aseptic meningitis, this result supported by other studies done in Egypt,<sup>(23)</sup> Portugal,<sup>(26)</sup> South Korea,<sup>(28)</sup> and in Nepal.<sup>(29)</sup>

The incidence and case-fatality rates of bacterial meningitis vary by region, country, pathogen, and age group. Without treatment, the case-fatality rate can be as high as 70 percent, and one in five survivors of bacterial meningitis may be left with permanent sequelae, including hearing loss, neurologic disability, or loss of a limb.<sup>(30)</sup> In our study, the overall case-fatality rate (CFR) for bacterial meningitis was 6.1% (3/49). The three cases occur only among bacterial meningitis cases and the age of the cases was less than two years. In two studies in Yemen and France, the CFR among bacterial meningitis was 10% and 9.2% respectively.<sup>(31,32)</sup> In contrast, a low rate of 3% recorded in USA during the pneumococcal conjugate vaccine era. That lower percentage recorded after the wider use of conjugate vaccines against pneumococcal infection, which has the potential to reduce the number of cases of invasive pneumococcal meningitis within a few years of implementation,<sup>(33)</sup> Clinical diagnosis of bacteria in human specimen depends, mainly, on several factors such as the number of organisms' present, prior use of antibiotics, and technique used for culturing the bacteria.<sup>(34)</sup> In Iraq, the antibiotics are usually available over the counter and therefore, patients have access and can receive a course of

antibiotics from a private practitioner or by the patient (him/her) without any physician prescription and/or laboratory tests. The percentage of positive cultures were 44.8 % (22/49), which is higher than two studies done in India and Nepal with a percentage of 25% and 36% respectively.<sup>(24,25)</sup> Culturing CSF specimen from partially treated patients lead to a lower yield of bacteria, particularly patients who have received antibiotic before lumbar puncture.

Among the isolated species, *Streptococcus pneumoniae* was the predominant organism with a percentage of 36.3%. Relatively high incidences of Pneumococcal infections were noted in many studies.<sup>(35,36,37)</sup> Although, *H. influenzae* and *N. meningitidis* considered as common pathogens causes bacterial meningitis in children; these bacteria were not detected from CSF culture during the period of this study. The possible explanations could be one of the followings: The conjugate vaccine against Hib (Haemophilus Influenzae Type B) was introduced in Iraq and provides long-lasting immunity. Also, these genera are fastidious organisms which require special requirements to grow on microbiological media, the diagnosis must be done by a trained professional technician. Moreover, maybe these two species are not truly prevalent in our country. Additionally, partially treated children before the performance of diagnostic lumbar punctures increases the number of false-negative cerebro-spinal fluid bacterial culture results.

The identification of the isolates at the level of species was doable due to the availability of the new automated system VITEK2 which identifies a wide variety of pathogenic bacteria. VITEK2 provides precise results at the level of species which cannot be identified by the conventional manual methods. Among the isolated species, two isolates identified as *Enterococcus faecium* and *Kocuria virians*. To our knowledge, this is the first emergence of these species as potential pathogens responsible for bacterial meningitis among our children. Our results show a percentage of 4.5 % for one isolate of *Enterococcus faecium*. Enterococcal meningitis is an uncommon disease, accounting for only 0.3% to 4% of cases of bacterial meningitis which is nevertheless associated with a high mortality rate. It has been described most often in patients with neurosurgical conditions like head trauma, shunt devices, or cerebro-spinal fluid leakage.<sup>(38)</sup> *Enterococcus faecalis* and *Enterococcus faecium* are the two species most frequently isolated during the course of meningitis.<sup>(39)</sup> The same percentage of 4.5 % for one isolate of *Kocuria virians* appeared among the 22 isolates. Now it's well known that *Kocuria* species are responsible for

different types of infection, mostly in immunocompromised hosts with serious underlying conditions.<sup>(40)</sup> Unfortunately, the shortage of the skill required and the facilities involved in the identification of *Kocuria* species lead to misidentification in many laboratories, commonly misidentified *Kocuria* isolates as *Staphylococci*<sup>(40)</sup> or *Micrococcus*.<sup>(41)</sup> Although the diseases caused by *Kocuria* species are mistakenly believed to be rare, it is suggested that physicians should not underestimate the importance of *Kocuria* spp when isolated from clinical samples.

In this study, the eight isolates of *S. pneumoniae* had high resistance against penicillin and Azithromycin. Moreover, these isolates had intermediate resistance against the third generation cephalosporin Ceftazidime. These results represent an alarming and disturbing rate of resistant pneumococcus species in our area. Penicillin-resistant pneumococcal meningitis have become common,<sup>(42)</sup> the prevalence is higher in isolates from hospitalized patients versus outpatients and higher in children compared with adults.<sup>(43)</sup> The penicillin resistant pneumococcus is usually also resistant to other common antibiotic such as macrolide, tetracycline, co-trimoxazole, chloramphenicol and clindamycin making the choice of antibiotic limited to the third generation of cephalosporin, vancomycin together with rifampicin in case of critical infection such as meningitis.<sup>(42)</sup> *Streptococcus pneumoniae* should be closely monitored because the highly resistance to many antibiotics is evolving rapidly locally and globally.<sup>(43)</sup> Yet, the resistance against vancomycin was not reported in our study, except one isolate of *Staphylococcus aureus*. In addition, the results indicated that the resistance of *E.coli* isolates against the third generation cephalosporins was considerable, also the two strains were resistant to Ampicillin. Many studies demonstrated that the rapid global rise of infections caused by *Escherichia coli* that are resistant to clinically relevant antimicrobials, including third-generation cephalosporins, is cause for concern.<sup>(44,45)</sup>

**Conclusion:** The current knowledge showed that positive parameters in analysis of CSF can be used to differentiate between bacterial and non-bacterial meningitis. However, we cannot exclude the possibility of a bacterial type meningitis even with a negative culture result. Also, using new technology for the identification of different species of bacteria is important to distinguish between pathogenic and non-pathogenic species which is regarded as a crucial step for management of the patients.

## REFERENCES

- 1- Charles G. and Nivedita S. (2016). Central Nervous System Infections. IN: Robert M. Kliegman, MD, Bonita F. Stanton, MD, Richard E. Behrman, MD. Nelson textbook of pediatrics. 20th ed. Philadelphia: ELSEVIER.:2936
- 2- Robertson CK, Dahlberg SE, Edberg SC. (1992). Clinical and laboratory analyses of cytospin-prepared Gram stains for recovery and diagnosis of bacteria from sterile body fluids. J Clin Microbiol. 30:377–80.
- 3- Ray P., Badarou-Acosi G., Viallon A. (2007). Accuracy of the cerebrospinal fluid results to differentiate bacterial from non-bacterial meningitis, in case of negative gram-stained smear. The American Journal of Emergency Medicine. 25 (2):179–184
- 4- Agier L., Broutin H., Bertherat E. (2013). Timely detection of bacterial meningitis epidemics at district level: a study in three countries of the African Meningitis Belt. Transactions of the Royal Society of Tropical Medicine and Hygiene. 107(1): 30–36.
- 5- Kim KS. (2009). New diagnostic and therapeutic options in bacterial meningitis in infants and children. Minerva Pediatr. 61(5):531-48.
- 6- Kala Yadhav ML. (2014). Study of Bacterial Meningitis in Children Below 5 Years with Comparative Evaluation of Gram Staining, Culture and Bacterial Antigen Detection. J Clin Diagn Res. 8(4):04–06.
- 7- Feigin R.D., Cutrer W.B. (2009). Bacterial meningitis beyond the neonatal period. In: Feigin and Cherry's Textbook of Pediatric Infectious Diseases, 6th ed, Feigin RD, Cherry J, Demmler-Harrison GJ, Kaplan SL (Eds), Saunders, Philadelphia. P: 439.
- 8- William Bonadio MD. (2014). Pediatric Lumbar Puncture and Cerebrospinal Fluid Analysis. J Emerg Med. 46 (1):141-150.
- 9- Roos K. L. (2003). Cerebrospinal fluid, in Principles of Neurologic Infectious Diseases, Roos K. L (Ed). McGraw-Hill. chapter 1, pp. 1–12.
- 10- Dubos F, Korczowski B, Aygun DA. (2010). Distinguishing between bacterial and aseptic meningitis in children: European comparison of two clinical decision rules. Arch Dis Child. 95:963–7.
- 11- Zimmerli W. (2005). How to differentiate bacterial from viral meningitis. Intensive Care Med. 31:1608–10.
- 12- Dalton H.P., Allison M.J. (1968). Modification of laboratory results by partial treatment of bacterial meningitis. Am J Clin Pathol. 49 (3):410–413.
- 13- Kanegaye J.T., Solimanazadeh P., Bradley J.S. (2001). Lumbar puncture in pediatric bacterial meningitis: defining the time interval for recovery of cerebrospinal fluid pathogens after parenteral antibiotic pretreatment. Pediatrics. 108 (5):1169–1174.
- 14- El Bashir H., Laundry M., Booy R. (2003). Diagnosis and treatment of bacterial meningitis. Arch Dis Child. 88 (7):615-20.
- 15- Koster R. R., Korshin A., Meyer C.N. (2008). Antibiotic treatment delay and outcome in acute bacterial meningitis. J infect. 57 (6):449-54.
- 16- Mosavi-Jarrahi A., Esteghamati A., Asgari F., Heidarnia M., Mousavi-Jarrahi Y, Goya M. (2009). Temporal analysis of the incidence of meningitis in the Tehran metropolitan area, 1999-2005. Popul Health Metr. 7:19.
- 17- Rao B.N., Mahdi I., Shembesh N.M., Bargathy S.M. (1998). Etiology and occurrence of acute bacterial

- meningitis in children in Benghazi, Libyan Arab Jamahiriya. *EMHJ*. 4(1):50-7.
- 18- Chinchankar N., Mane M., Bhav S., Bapat S., Bavdekar A., Pandit A.(2002). Diagnosis and outcome of Acute Bacterial Meningitis in early childhood. *Indian Paediatrics*. 39: 914-21
- 19- Green M. (1992).The male predominance in the incidence of infectious diseases in children: a postulated explanation for disparities in the literature. *Int J Epidemiol*.21(2):381–386.
- 20- McNeil J.R. (1966). Acute bacterial meningitis as seen in children of Eastern Saudi Arabia. *Clin Pediatr* .5:437-8.
- 21- Babiker M.A., Taha S.A. (1984). Meningitis in children of Riyadh. *J Trop Med Hyg* .87:245-8.
- 22- Abomelha A., Uduman S.A., Saleh M.F.( 1988). Childhood bacterial meningitis. *Ann Saudi Med*.8:274-8.
- 23- Rabab F.,1Marwa K.,1 Waleed F.(2014).Role of Clinical Presentations and Routine CSF Analysis in the Rapid Diagnosis of Acute Bacterial Meningitis in Cases of Negative Gram Stained Smears . *Journal of Tropical Medicine*. Article ID 213762.
- 24- Negrini B., Kelleher K.J., Wald E.R. (2000).Cerebrospinal fluid findings in aseptic versus bacterial meningitis. *Pediatrics*.105:316–319.
- 25- Peltola H.( 2001). Burden of meningitis and other severe bacterial infections of children in Africa: implications for prevention. *Clin. Infect Dis* 32: 64–75.
- 26- Sofia Á., Teresa C., Ana M. (2013). Prediction of bacterial meningitis based on cerebrospinal fluid pleocytosis in children.The *Brazilian Journal of Inf. Digno*.17 (4):401–404.
- 27- Mayah W.W., El-Yamany S., Jimani A., El-aadany S.,Hassanien M., Hasan A.(2013). Study of different diagnostic markers used to differentiate septic from aseptic meningitis. *J Microscopy and Ultrastructure* 1:35-42.
- 28- Jungpyo L., Hyeen K., Joon S. L., Heung D. K., Hoon-Chul K.(2015). Applying the bacterial meningitis score in children with cerebrospinal fluid pleocytosis: a single center's experience. *Korean J Pediatr*. 58(7):251-255.
- 29- Kalpana K. M., Tejesh M., Seshagiri R., Sahisnuta B., Ravi S.(2013). Is Cerebrospinal Fluid C-reactive Protein a Better Tool than Blood C-reactive Protein in Laboratory Diagnosis of Meningitis in Children? *Sultan Qaboos University Med J*. 13, Iss. 1: 93-99.
- 30- Rosenstein N. E., B. Perkins A., Stephens D. S., Popovic T.(2001). Meningococcal Disease. *New England Journal of Medicine*.344:1378-1388.
- 31- Al Khorasani A. and Banajeh S. (2006).Bacterial profile and clinical outcome of childhood meningitis in rural Yemen: a 2-year hospital-based study. *J Infect*. 53(4):228-34.
- 32- Bingen1E., Levy C., La Rocque F., Michel Boucherat M.,Emmanuelle Varon E., Alonso J.M., Dabernat H. (2005). Bacterial Meningitis in Children: A French Prospective Study. *Oxford Journals Medicine & Health.Clinical Infectious Diseases*Volume 41(7): 1059-1063.
- 33- Nigrovic L.E., Kuppermann N., Malley R. (2008). Children with bacterial meningitis presenting to the emergency department during the pneumococcal conjugate vaccine era. *Acad Emerg Med*.15(6):522-8.
- 34- Mani R., Pradhan S., Nagarathna S., Wasiulla R., and Chandramuki A. (2007). Bacteriological profile of community acquired acute bacterial meningitis: a ten-year retrospective study in a tertiary neurocare centre in South India,*Indian Journal of Medical Microbiology*.25(2):108-14.
- 35- Grimwood K., Anderson P., Anderson V., Tan L., Nolan T. (2000). Twelve year outcomes following bacterial meningitis: further evidence for persisting effects. *Arch Dis Child*.83(2):111–6.
- 36- Bhat B.V., Verma I.C., Puri R.K., Srinivasan S., Nalini P. (1991). A profile of pyogenic meningitis in children. *J Indian Med Assoc*.89 (8):224–7.
- 37- Al Khorasani A. and Banajeh S.(2006). Bacterial profile and clinical outcome of childhood meningitis in rural Yemen: a 2-year hospital-based study. *J Infect*.53(4):228-34.
- 38- Pintado V., Cabellos C., Moreno S., Meseguer M.A, Ayats J., Viladrich P.F. (3003). Enterococcal meningitis: a clinical study of 39 cases and review of the literature. *Medicine (Baltimore)* .82:346-64.
- 39- Gascon F., Castano M.A., Gonzalez A. (2003). Cordon MD: Endocarditis due to *Enterococcus casseliflavus*. *Infecc Microbiol Clin* .21:275-276.
- 40- Dotis J., Printza N., Stabouli S., Papachristou F. (2015). *Kocuria* species peritonitis: although rare, we have to care.35 (1):26-30.
- 41- Savini V., Catavittello C., Masciarelli G. (2010). Drug sensitivity and clinical impact of members of the genus *Kocuria*. *J Med Microbiol*.59:1395–402.
- 42- Klugman K.P.(1990). Pneumococcal resistance to antibiotics. *Clin Microbiol Rev* 3:171–96.
- 43- Stephanie J. S. and Bernard B. (2001). Resistant pneumococcal infections: the burden of disease and challenges in monitoring and controlling antimicrobial resistance. *WHO/CDS/CSR/DRS*.6.
- 44- Elisabeth M., Frank S., Barbara S.B., Petra G. (2010). Research Dramatic increase of third-generation cephalosporin-resistant *E. coli* in German intensive care units: secular trends in antibiotic drug use and bacterial resistance, 2001 to 2008. *Critical Care J*. 14:113.
- 45- Yoon S. P., Daniel M. Y., Laura E. J., Ameet H., James S. L., James H. J., Yohei D. (2012). Clinical and Microbiologic Characteristics of Cephalosporin-Resistant *Escherichia coli* at Three Centers in the United States .*Antimicrob Agents Chemother*. 56(4): 1870–76.