IGM Publication

Journal of Medical Science and Clinical Research
Volume||1||Issue||3||Pages130-140||2013
Website: www.jmscr.igmpublication.org ISSN (e): 2347-176X

Epidemiological and Clinical Study of Bacterial Meningitis in Menoufiya Governorate

[1]Alif A. Alam, [2]Wesam S. Morad, [3]Mohamed H. Bahbah and [4]Azza Z. Labeeb

Email: wesammorad@yahoo.com

[1] Pediatric Hepatology department; [2]Environmental Health of Liver department, National Liver Institute, Menoufiya University, [3] Pediatric department, [4]Microbiology and Immunology department, Faculty of Medicine, Menoufia University

ABSTRACT:

Bacterial meningitis in children is associated with substantial excess risk of intellectual, cognitive, and auditory impairment that persists into adolescence. Continuing developmental problems of higher order language, organisation, problem solving, and central auditory function may increase learning and behavioral difficulties. The aim of this study was to evaluate clinical, laboratory and epidemiology of bacterial meningitis in Menoufiya Governorate Fever Hospitals.

Key words: *Bacterial meningitis; CSF; H. influenza; Gram stain; N. meningitides; Pneumococci.*

Introduction

Bacterial meningitis (BM) is a severe infection of the central nervous system which occurs especially in children <5 years of age. Although the occurrence of negative consequences of BM in developed countries is strongly reduced by vaccination strategies, antibiotic treatment and good care facilities, BM is still responsible for substantial morbidity and mortality in both developing and developed countries *(1).*

Bacterial meningitis in children is associated with substantial excess risk of intellectual, cognitive, and auditory impairment that persists into adolescence. Continuing developmental problems of higher order language, organisation, problem solving, and central auditory function may increase learning and behavioral difficulties. The risk of these adverse outcomes is greatest in, but not confined to, those who experienced acute neurological complications at the time of their illness *(2).*

The mortality rate is approximately 5%, and the long-term morbidity, mainly consisting of persistent neurological sequelae, is 15% *(3).* Sensorineural hearing loss, seizures, motor problems, hydrocephalus and mental retardation *(4),* as well as more subtle outcomes like cognitive, academic and behavioral problems are observed in post-meningitis children *(5).*

Because of the high mortality rate and long-term sequels, fast and accurate diagnosis and appropriate treatment of acute bacterial meningitis (ABM) are fundamental for a good outcome *(6).* The initial antibiotic regimen is usually empirical, and therefore, knowledge of the epidemiological profile of ABM in the community could lead to the best therapeutic choice *(7).*

Clinical signs and symptoms are unreliable in distinguishing bacterial meningitis from the more common forms of aseptic meningitis; therefore, a lumbar puncture with cerebrospinal fluid analysis is recommended *(8).*

Meningitis is considered as an endemic disease in Egypt. Apart from endemicity, a violent periodic epidemic occurs every 6-12 years in the African meningitis belt *(9).*

Endemic meningitis among children takes the form of sporadic cases or small clusters with an endemicity rate of 1.5/100,000 and 20/100,000 population in the developed and developing countries, respectively *(10).*

At least 890,000 cases [500,000 in Africa; 210,000 in pacific countries; 100,000 in Europe and 80,000 in America] are estimated to occur annually. Of these cases, 160,000 and 135,000 of them are disabling and fatal, respectively *(11).*

Aim of work: is to evaluate clinical, laboratory and epidemiology of bacterial meningitis in Menoufiya Governorate Fever Hospitals.

Patients and methods:

The study was designed to include all patients clinically suspected to have meningitis and admitted to Menoufia Governorate fever hospitals in the time period from 1st January 2010 to 31st December 2011. The fever hospitals were selected based on being reference hospitals in its area.

- **Inclusion criteria**

- Clinical description:

Bacterial meningitis manifests most commonly with fever, headache and stiff neck. The disease may progress rapidly to shock and death. However, other manifestations may be observed. For infants: fever accompanied by bulging fontanel.

- Laboratory Criteria for Diagnosis

Isolation of a bacterial species from the cerebrospinal fluid.

- **Exclusion criteria :**

All patients that had been diagnosed repeatedly with events of bacterial meningitis due to structural defects of the CNS, as well as patients younger than one month old and older than 15 years old. Also all patients that not have symptoms and signs of CNS infection.

- The children (Total number 279) were divided into groups according to age as follows: Group A (Infant): from one month to one year (n=130; 75 boys, 65 girls), Group B (Preschool children): from one

year to five years (n=64; 32 boys, 32 girls) and Group C (school children): from five years to fifteen years (n=85; 49 boys, 36 girls).

- **Methodology:**

1) A Standardized data collection questionnaire was developed to collect both

- Epidemiological data: age, gender, place of residence, occupation of the mother, onset date, admission date, prior antibiotic treatment, and
- Clinical data: presence of the following manifestations on admission (fever, seizures, nausea/vomiting, diarrhea, headache, skin rashes or lesions, stiff neck, bulging fontanel in infants less than 1 year old).

2) Collection of samples from all patients: *(12)*

- **Blood samples:** Diphasic blood culture bottles (bio Merieux) were used. Blood were aseptically withdrawn, 2 ml from young children. The needle was inserted through the rubber liner of the bottle cap *(13).*
- **Cereprospinal fluid (CSF) samples through lumber puncture:** collection of CSF is an invasive technique and should be performed by experienced personnel under aseptic conditions. If meningitis is suspected CSF is the best clinical specimen to use for isolating and identifying the etiological agents. The collection of CSF should be performed for diagnosis only. CSF should be inoculated directly onto both a supplemented chocolate agar plate (CAP) and a blood agar plate (BAP).

3) Gram stain procedure for CSF of all patents: (Hucker Modification)

A presumptive diagnosis of BM caused by H, influenzae, ST. pneumoniae and N. meningitides can be made by gram stain of the CSF sediment. In which:

- **N. meningitides** may occur intra- or extra-cellularly in the polymorphnuclear Leukocytes and will appear as Gram-negative, coffee-bean-shaped diplococcic
- **ST. pneumoniae** are lanceolate, Gram-positive diplococci sometimes occurring in short chains.
- **H. influenzae** are small, pleomorphic Gram-negative rods or coccobacilli with random arrangement.

4) Inoculation of Primary Culture Media :

- Blood samples *(13).*

- CSF: Is the best medium for ST. pneumoniae is a BAP. For H. influenzae a CAP supplemented with haemin and a growth supplement such as IsoVitaleX, should be used. N. meningitides grows on both BAP and CAP.

5) Identification of the isolates :

a- Identification of ST. pneumoniae

- Gram stain: gram-positive cocci arranged in pairs and short chains.

- Small translucent, pin point colonies on blood agar medium and most of them produce haemolytic effect on blood agar.
- Streptococci are catalase test negative.

b- Identification of N. meningitides

- Gram stain: gram-negative, bean shaped diplococci.
- From growth on a BAP, perform Kovac's oxidase test. The oxidase test determines the presence of cytochrome oxidase. Results confirmed with carbohydrate reactions.

c- Identification of H. influenzae

- Gram stain: small, pleomorphic gram-negative rods or coccobacilli with random arrangements.
- Identification of X and V factor requirements: H. influenzae will grow only around the disk containing both X and V factors.

- **Data management** :

The data collected were tabulated & analyzed by SPSS (statistical package for the social science software) statistical package version 16 on IBM compatible computer.

Quantitative data were expressed as mean & standard deviation (X±SD) and analyzed by applying **Student's t-test** for comparison of quantitative variables**. F test (ANOVA) test** was used as a test of significance for comparison between more than two means.

Qualitative data were expressed as number and percentage (No & %) and analysed by applying **chi-square test**.

All these tests were used as tests of significance at $P < 0.05$.

Results:

Headache is often associated with Pneumococci and is significantly higher in Pnumococci than H.influenzae and Meningococci while vomiting is often associated with Pneumococci and is significantly higher in Pneumococci than Meningococci and H.influenzae. Irritability and refusal of feeding are often associated with Meningococci and significantly higher in Meningococci than H.influenzae and Pneumococci. Seizures are often associated with H.influenzae and significantly higher in H.influenzae than Meningococci and Pneumococci. Meningeal irritation signs are often associated with Pneumococci and significantly in Pneumococci than H.influenzae and Meningococci. Bulging anterior fontanel is often associated with Meningococci and significantly higher in Meningococci than H.influenzae and Pneumococci. Skin rash is associated with Meningococci than other organisms.

Discussion:

Bacterial meningitis (BM) is a severe infection of the central nervous system which occurs especially in children < 5 years of age. Although the occurrence of negative consequences of BM in developed

countries is strongly reduced by vaccination strategies, antibiotic treatment and good care facilities, BM is still responsible for substantial morbidity and mortality in both developing and developed countries *(1)*.

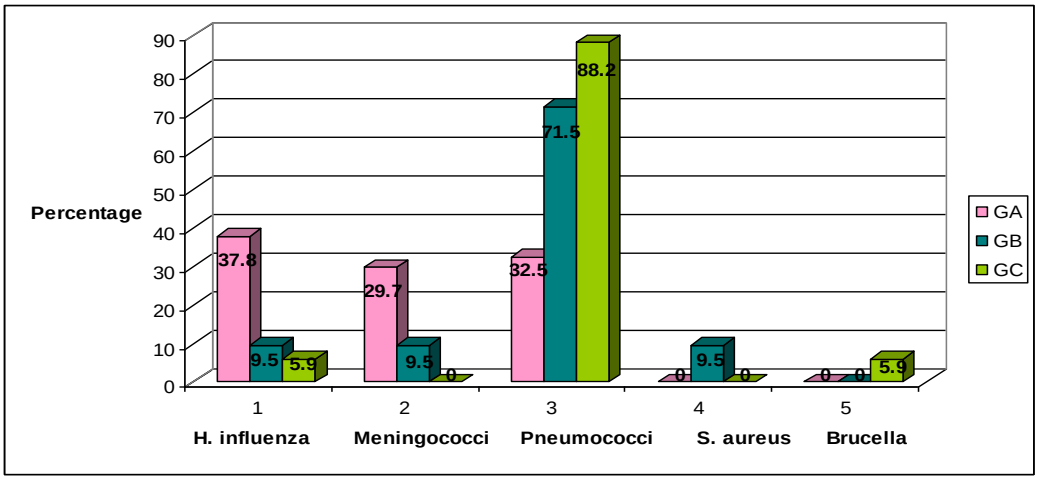


Figure (1): Comparison between three studied groups regarding positive culture.

Table (1) comparison between three studied groups regarding socio- demographic data.

Group A = Infant.** Group B =AFTER I year till 5 years = pre school age.** Group C= More than 5 years = school age

Socio demographic data	Group A (N=130) N	%	Group B (N=64) N	%	Group C (N=85) N	%	p-value
Sex :							
Male	75	57.7	32	50.0	49	57.6	> 0.05
Female	55	42.3	32	50.0	36	42.4	
Residence :							
Rural	71	54.6	30	46.9	42	49.4	> 0.05
Urban	59	45.4	34	53.1	43	50.6	
Mothers work :							
House wife	108	83.1	50	78.1	60	70.6	> 0.05
Clerk	22	16.9	14	21.9	25	29.4	

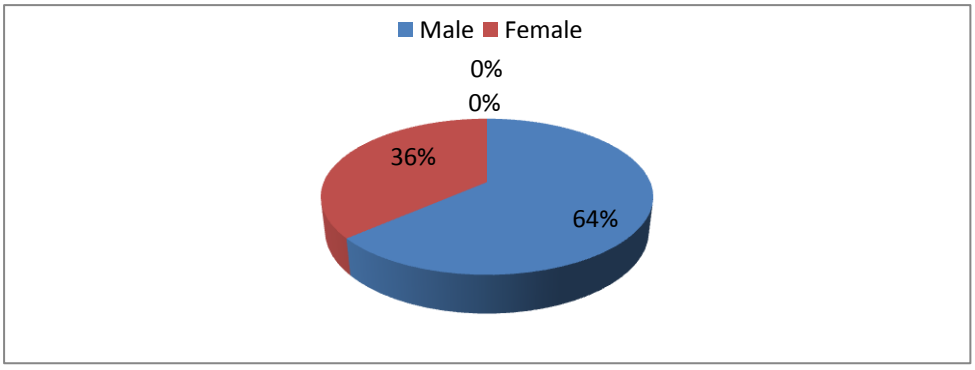
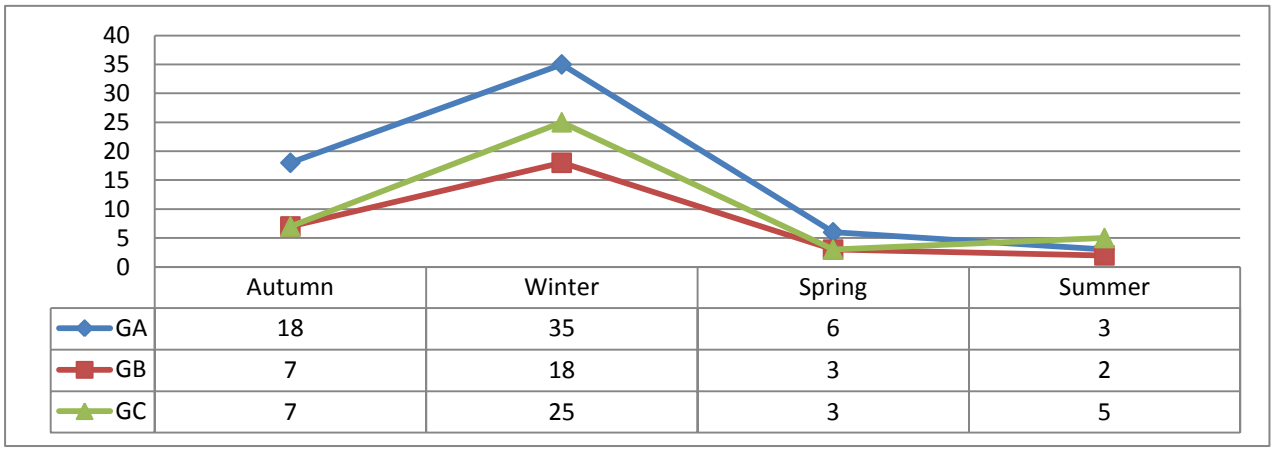


Figure (2): Male to Female ratio in confirmed cases of BM.



	Autumn	Winter	Spring	Summer
GA	18	35	6	3
GB	7	18	3	2
GC	7	25	3	5

Figure (3): Comparison of three studied groups regarding season of infection

In this study the main three causative bacteria were N. meningitides, H. influenzae and ST. pneumoniae. Similar findings were reported by *(14),* who found that the three primary causative organisms involved in causing community-accquired bacterial meningitis in children from Kosova were (N. meningitides, H. influenzae and ST. pneumoniae).

Also similar findings were reported by ***Luca et al.,*** *(15)* ***and Youssef et al.,*** *(16)* who found that the main three causative organisms were (N. meningitides, H. influenzae and ST. pneumoniae).

In the current study **(table 3)** as shown in infants less than one year H. influenzae was the leading cause of bacterial meningitis resulting in (14/37) (37.8%) of cases in this age group. This is in agreement with ***Silva et al.,*** *(17)* who found in their study that the most common etiologic agent of bacterial meningitis in infants under the age of 1 year was H. influenzae (42.2%). ***Miranzi et al.,*** *(18)* in a review of bacterial meningitis in children, also reported that H. influenzae was the most frequent cause of bacterial meningitis in infants < 1 year.

As regards meningitis due to H. influenzae we found that (14/ 37) (37.8%) were below 1 year. ***Silva et al.,*** *(17)* reported that (68%) of H. influenzae meningitis cases occurred in infants less than 1 year old.

Silva et al., *(17)* reported that the frequency of isolation of the same organism in the age group (<1 year, 1-5 years, 5-15 years, and >15 years) was about (38.9%), (44.8%), (49.0%), and (50.0%) respectively.

In the present study H. Influenza was the leading cause of meningitis in the age group below 1 year and N. meningitides with Staph aureus were the second leading cause of meningitis in the age group 1 years to less than 5 years old (9.5%) & (9.5%) respectively, while S. pneumoniae was the leading cause above this age (35.3%) similar findings were reported by *(19).*

In the present study **(table 2),** the overall male to female ratio in all suspicious cases was approximately 1.27:1. But the male to female ratio in positive cases for bacterial meningitis was 1.75:1. This is in accordance with many other studies conducted in Egypt documenting that males are more exposed to infection than females and the male to female ratio ranged from as low as 1.1:1 to as high as 2.8 : 1. ***Abro***

et al., *(20)* noted that the rate of infection in males (55.7%) was higher than females (44.3%) with male to female ratio 1.3:1; very similar to the ratio in the present study. ***François et al.,*** *(21)* reported the rate of infection in males (55%) was higher than females (45%) with male to female ratio 1.2:1 very similar to the ratio in the present study. One of the explanations given for male predominance found by ***Abdel Gawad et al.,*** *(22)* who found in their study that males (64%) were more susceptible than females (36 %) with a significant difference.

Table (2) shows Male to Female ratio between the three studied groups

Gender	Group A (N=130)		Group B (N=64)		Group C (N=85)		p-Value
	N	%	N	%	N	%	
Male	75	57.4	32	50.0	49	57.6	>0.05
Female	55	42.6	32	50.0	36	42.4	

Pediatr Crit Care Med; 7: GA (N=130)=Male to Female ratio 75/55(1.36:1)

GB(N=64)=Male to Female ratio 32/32(1:1)
GC(N=85)=Male to Female ratio 49/36(1.36:1)

In the present work when considering sex prevalence among different categories, males were more than females in all etiologic groups. The highest ratio of male prevalence was recorded for meningitis due to N. meningitides 2:1; ST. pneumoniae 1.7:1 and H. influenzae 1.25:1.

Weiss et al., *(23)* found that (58.4%) of cases were males with male to female ratio 1.4 : 1, the percent of cases that were males with H. influenzae, N. meningitides and ST. pneumoniae were (53.8%), (54.7%) and (57.1%) with male to female ratios (1.1 : 1), (1.2 : 1) and (1.3 : 1) respectively. For cases due to other etiologies the ratio was (1:1). No statistically significant difference was observed in their study among different etiologies of bacterial meningitis regarding sex distribution.

Santos et al., *(24)* in their study on meningococcal meningitis reported male to female ratio 2.4:1. ***François et al.,*** *(19)* stated that generally speaking males are more affected than females and this may be due to the fact that males are more active and movable than females.

We noted in our study that, there was significant association between the age of the patients and the type of isolated organism, as the relative frequencies of the different bacterial species causing acute bacterial meningitis differed among infants, preschool, and school aged children. This is in accordance with ***Silva et al.,*** *(15)* reporting that the relative frequencies with the different bacterial species that cause meningitis are related to the place and age of the patients. Also ***Silva et al.,*** *(15)* stated that population based studies in Brazil from 2005 to 2008 as well as their study clearly showed that the relative importance of pathogens

causing meningitis differs according to age. In Egypt ***Dorgham,*** *(25)* also reported that age of the patient influences to a great extent the type of causative organism of meningitis **(table 3).**

Table (3) Comparison between the studied groups regarding positive culture :

Positive culture	GA (130) (N = 37)		GB (64) (N= 21)		GC (85) (N= 34)		p-value
	N	%	N	%	N	%	
H.influenzae	14	37.8	2	9.5	2	5.9	< **0.01**
Meningococc	11	29.7	2	9.5	0	0.0	< **0.01**
Pneumococci	12	32.5	15	71.5	30	88.2	< **0.01**
S. aureus	0	0.0	2	9.5	0	0.0	< **0.05**
Brucella	0	0.0	0	0.0	2	5.9	> 0.05

The prevalence of Pneumococci is significantly higher among school aged group than other groups 30/34 (88.2%), (P < 0.01). While H.influenzae was the leading cause below one year age 14/37 (37.8%).

Coinciding with the results of the present study in **(table 4)** ***CDC,*** *(11)* stated that bulging of the fontanel, a sign of increased intracranial pressure, is of great diagnostic value. They also reported that vomiting is more marked in infants and young children. ***François et al.,*** *(19)* reported that seizures were more frequent among infants than in older age groups with a highly significant difference between them and they also reported that headache was more prominent with adults than in the younger age with statistically significant difference too. ***Silva et al.,*** *(15)* also noted the higher occurrence of seizures in younger age groups while headache was more prominent in older age groups. ***François et al.,*** *(19)* reported headache was prominent in older age while vomiting was prominent in younger age groups. ***Sunit and Arun,*** *(26)* suggested that the absence of headache in some patients with bacterial meningitis may be attributed to the fact that infants are unable to localize this compliant.

Table (4) Difference of symptoms and signs between different bacterial causes

Parameter	H. influenzae (N=18)		Meningococci (N=13)		Pneumococci (N=57)		P-value
	N	%	N	%	N	%	
High Fever	18	100.0	13	100.0	57	100.0	-
Headache	2	11.1	0	0.0	27	47.4	< **0.01**
Vomiting	10	55.6	8	61.5	43	75.4	< **0.01**
Irritability	12	66.7	7	53.8	9	15.8	< **0.05**
Refusal of feeding	10	55.6	6	46.2	9	15.8	< **0.05**
Coma	4	22.2	2	15.4	5	8.8	< **0.05**
Seizures	10	55.6	7	33.3	11	19.3	< **0.05**
Neck stiffness	2	11.1	0	0.0	29	50.9	< **0.01**
Bulging ant fontanel	10	55.6	9	69.2	5	8.8	< **0.05**
CNS Palsy	0	0.0	0	0.0	4	7.02	> 0.05
Skin rash	2	11.1	7	53.8	15	26.3	< **0.01**

Conclusion:

We found that the three major pathogens accounting for (95.7%) of bacterial meningitis in Menoufiya Governorate fever hospitals were ST. pneumoniae, N. meningitides and H. influenzae. On which ST. pneumoniae has been the most frequent isolated organism causing bacterial meningitis. In infants less than 1 year, H. influenzae was the most common etiologic agent while the age group 1 year to less than 5 years, H. influenzae , N. meningitides, and ST. pneumoniae had nearly caused similar percentages of cases . Other group of children aged from 5-15 years, ST. pneumoniae was the most common etiologic agent of bacterial meningitis. Bacterial meningitis is more common in males than females. Some clinical manifestations when present are more likely to indicate specific type of infection as rash and petechiae suggesting meningococcal infection. Seasonal variation regarding bacterial meningitis cases was demonstrated in this study with the highest incidence in autumn and winter.

References:

1. **Theodoridou MN, Vasilopoulou VA, Atsali EE, et al.:** "Meningitis registry of hospitalized cases in children: epidemiological patterns of acute bacterial meningitis throughout a 32-year period". BMC Infect Dis. 2007; 7:101.
2. **Grimwood K, Anderson P, Anderson V, et al.:** "Twelve year outcomes following bacterial meningitis: further evidence for persisting effects". *Arch Dis Child* 2000; 83:111–16.
3. **Pelkonen T, Roine I, Monteiro L, et al.:** "Risk factors for death and severe neurological sequelae in childhood bacterial meningitis in sub-Saharan Africa". Clin Infect Dis. 2009; 48:1107–1110.
4. **Koomen I, Grobbee DE, Roord JJ, et al.:** "Hearing loss at school age in survivors of bacterial meningitis: assessment, incidence, and prediction Pediatrics". 2003; 112:1049–1053.
5. **Anderson V, Anderson P, Grimwood K, et al.:** "Cognitive and executive function 12 years after childhood bacterial meningitis: effect of acute neurologic complications and age of onset. J Pediatr Psychol". 2004; 29:67–81.
6. **Salih MA, Khaleefa OH, Bushara M, et al.:** "Long term sequelae of childhood acute bacterial meningitis in a developing country. A study from Sudan". Scand J Inf Dis 1991; 23:175-182.
7. **Mantese OC, Hirano J, Santos IC, et al.:** "Perfil etiológico das meningites bacterianas em crianças". J Pediatr 2002; 78:467-474.
8. **Bamberger DM:** "Diagnosis, initial management, and prevention of meningitis.Am Fam Physician". 2010; 82(12):1491-8.

9. **Tikhomirov E, Santa MM, Eastern K:** "Meningococcal diseases; Public health burden and control". *Wld hlth Statist Quart* 1997; 50: 170-7.
10. **World Health Organization:** "Control of epidemic meningococcal diseases". WHO practical guidelines. World Health Organization and Foundation Marcel Merieux, Edition Foundation Marcel Merieux, Lyon 1995.
11. **Centers for Disease Control and Prevention**: "Causes [online]". Retrieved January 13, 2010. From http://www.cdc.gov/meningitis/about/causes.html.
12. **Koneman EW, Winn WC, Allen SD, et al.:** *Koneman's Color Atlas and Textbook of Diagnostic Microbiology*, 6th edition. Baltimore, MD: Lippincott Williams and Wilkins, 2006.
13. **Cheesbrough Monica:** "District laboratory practice in tropical countries". Volume II. Bath Press. Great Britain 2001.
14. **Ceyhan M, Yilidirim I, Balmar P:** "Etiology of Childhood Acute Bacterial Meningitis". Turkey. Emerg Inf Dis 2008; 14(7):1089-1096.
15. **Luca V, Gessner BD, Luca C, Turcu T, Rugina S, Ilie M, Novakova E, Vlasich C:** "Incidence and etiological agents of bacterial meningitis among children < 5 years of age in two districts of Romania". *Eur J Clin Microbiol Inf Dis.* 2004; 23:523-8.
16. **Youssef FG, El-Sakka H, Azab A, Eloun S, Chapman GD, Ismail T, Mansour H, Hallaj Z, Mahoney F:** "Etiology, antimicrobial susceptibility profiles, and mortality associated with bacterial meningitis among children in Egypt". *Ann Epidemiol* 2004, 14(1):44-8.
17. **Silva WA et al.:** "Acute bacterial meningitis in northeastern Brazil Revista da Sociedade Brazileira de Medicina Tropical"; 2010; 43(4):455-457.
18. **Miranzi S, Camacho LA, Valente JG.:** "Haemophilus influenzae type b: epidemiological ...". 2006 Aug; 118(2):e421-9.
19. **Brandileone MCC, Casagrande ST, Guerra ML, Zanella RC, Andrade AL, Di Fabio JL:** "Increase in numbers of beta-lactam-resistant invasive Streptococcus pneumoniae in Brazil and the impact of conjugate vaccine coverage". J Med Microbiol 2006; 55:567-574.
20. **Abro AH., Abdou AS., Ali H., et al.**: "Cerebrospinal fluid analysis – acute bacterial versus viral meningitis" Pak J Med Sci; 2008, 24(5):645-650.
21. **François Dubos., Bartosz Korczowski., et al.:** "Serum Procalcitonin Level and Other Biological Markers to Distinguish Between Bacterial and Aseptic Meningitis in Children" Arch Pediatr Adolesc Med. 2008; 162(12):1157-1163.
22. **Abdel Gawad A, El-shazly S, Rakha A, El-Khateeb S:** "Annals of Clinical Microbiology and Antimicrobials", 2001; 286(6):688-93.

23. **Weiss DP, Coplan P, Guess H:** "Epidemiology of bacterial meningitis among children in Brazil, 1997-1998". Rev Saude Publica 2001; 35(3):249-55.

24. **Santos ML, Ruffino-Netto A:** "Meningococcal disease; epidemiological profile in the Municipality of Manus, Amazonas, Brazil, 1998/2002". Cad Saude Publica 2005; 21:823-829.

25. **Dorgham SH:** "Incidence and causative organisms of meningitis in Alexandria". Tanta Medical Journal 1989; 17:2219-2229.

26. **Sunit C, Arun Bansal:** "Serum cortisol level in children with acute and aseptic meningitis". 2006;