Epidemiology and Risk Factors Associated with Developing Bacterial Meningitis among Children in Gaza Strip

*Abdel Moat Al JAROUSHA,* Ahmed Al AFIFI

1. Dept. of Laboratory Medicine, Al Azhar University, Gaza, Palestine
2. Al Nasser Pediatric Hospital, Ministry of Health, Gaza, Palestine

*Corresponding Author: E-mail: amoati2007@yahoo.com

Introduction

Acute bacterial meningitis (ABM) is an important cause of childhood mortality and those who survive are at a higher risk of developing permanent neurological disability. Worldwide meningitis was estimated to cause 1, 73, 000 deaths in 2002, most of them were children from the developing world (1). In the high-mortality countries of the eastern Mediterranean region bacterial meningitis accounted for 23,000 (2.5%) of the 0.96 million deaths caused by infectious diseases in the region and contributed 13.3% of death due to meningitis worldwide (1). The annual incidence of bacterial meningitis in USA before the introduction of Hib conjugate vaccines was between 30-70/100 000 (2). Bacterial meningitis affects 35.000 Europeans each year and has a mortality rate of about 20% (3). In 2011 in Poland, it was recorded 2915 cases of meningitis and/or encephalitis. This included 1438 cases of viral etiology, 888 of bacterial etiology (4). There is variation in the incidence of bac-
tial etiological agents in different countries. A study conducted in Europe and Mediterranean region during 2007 found that Neisseria meningitidis, Streptococcus pneumoniae and Haemophilus influenzae type b were most commonly associated with bacterial meningitis accounting for almost 90% of reported cases of acute bacterial meningitis in infants over 60 days of age and young children(5). In contrast, another study was carried out in eastern of Mediterranean region during 2005-2010 found that the most commonly isolated pathogens were S. pneumoniae (27% of confirmed cases), N. meningitidis (22%), and H. influenzae (10%) (6). In the Middle East region different studies have been carried out in order to estimate the rate of infection and to find out the etiological agents. Accordingly N. meningitides, H. influenzae and S. pneumoniae were the predominant pathogens with different proportions (7-10). During the last two decades witnessed major advances in the understanding of the etiology and pathophysiology of bacterial meningitis; however, the major breakthrough was in the prevention of meningitis with the introduction of the Hib conjugate vaccine in the early 1980s. This resulted in a significant decrease in the incidence of bacterial meningitis in areas where routine vaccination of infants was instituted (11-12). Although diagnostic performance has recently improved by using new diagnostic methodologies (13, 14), the immediate management is usually decided upon treatment before a certain diagnosis is known and started considering only simple findings of cerebrospinal fluid (CSF) examination. At this time, the emphasis is to firstly not miss a bacterial with antibiotics or inappropriately prescribe corticosteroids for an uncontrolled viral infection. This decision can be difficult to make since CSF results often overlap between the two categories (15, 16). In order to help to distinguish bacterial and viral meningitis, academic algorithms (17, 18) and scoring tools have been proposed (19).

In Gaza Strip, few studies conducted to emphasis the etiologic agents of bacterial meningitis with the risk factors, therefore this study aimed to find out the different bacterial agents and the risk factors might be contributed in the development of such infection.

Materials and Methods

From January to December 2009, active surveillance of acute bacterial meningitis among children admitted to Gaza strip pediatrics hospitals was undertaken. Gaza Strip was divided into 5 geographic areas (Governorates). North and middle geographic regions were selected to represent the population characteristics of the country. Two hospitals, Al Nasser and Al Dora hospitals were selected to participate in the survey. These centers serve ≈62% of the entire pediatric population of Gaza strip. Approval was obtained from the Ethical Committees of the participating centers and Ministry of Health. In each hospital, suspected cases of acute bacterial meningitis were identified by using inclusion Criteria used for of identification of bacterial meningitis cases, the presence of a clinical picture compatible with bacterial meningitis and cerebrospinal fluid (CSF) neutrophilic pleocytosis of at least 100 neutrophil per cubic mm (presumptive) and then confirmed positive CSF culture for bacterial agents (20). The clinical symptoms were diagnosed by a pediatrician based on the following criteria: any sign of meningitis: fever [axillaries measurement >38°C], vomiting [≥3 episodes in 24 h], headache, meningeal irritation signs [bulging fontanel, Kernig or Brudzinski signs, or neck stiffness] in children >1 year of age fever without any documented source; impaired consciousness (Blantyre Coma Scale <4 if <9 months of age and <5 if >9 months of age). For each suspected case, demographic data were recorded by using a standardized questionnaire approved by experts in Pediatrics.

Epidemiology and statistics

Demographic data collected included age and sex, house crowdness the residents in a house rooms with two categories a-<3 individual per room and b->3 individual per room, mother education (elementary, secondary schools and university), malnutrition (anemia), family income (low, moderate and high according to local master of living). In the hospitals, sterile CSF was placed in suitable transport or holding media (usually trypticase soy
broth or thioglycollate broth), and rushed to the hospital laboratory that works 24 hr a day. All CSF samples received at the laboratory were processed immediately. The macroscopic appearance of the CSF was recorded. A total count of CSF cells and differential count were done using a haemocytometer and standard methods. The CSF samples were subjected to centrifugation, the resultant smear was Gram stained and examined microscopically. The procedure used for microbiological analysis was sediment from a centrifuged CSF specimen cultured on specific culture media, the isolated pathogens were identified by specific biochemical tests, API system and specific antisera. The biochemical tests used for detection of Bacterial meningitis in CSF were Glucose level and Protein level. The CSF-total-blood glucose and protein were computed. The Chi square and Odds ratio tests were applied to examine any significant association that may exists between each of the demographical, clinical development of Bacterial infection. Also Anova test was used to find out the impact of the three main pathogens on development of Anemia and Leukocytosis.

**Results**

Out of the 1853 suspected cases bacterial meningitis based on inclusion criteria with presence of cells >100 in CSF and were confirmed by culture in 73(3.9%) patients. Table 1 shows the age distribution and the Gender of the suspected cases. The data obtained demonstrated that there were 45(62%) males and 28(38%) females. Male to female ratio was 1.6:1.0, 42% of the cases were male less than 2 years while 80% of the cases were male less than 4 years. At the same time, 46% of the cases were female less than 2 years while 82% were female less than 4 years of age.

Table 2 illustrates the causative organisms *N. meningitides* (47.9%), *S. pneumoniae* (15.1%), *H. influenzae* (13.7%), *E. coli* (11.0%), *Enterobacter* sp. (6.8%), *Citrobacter* sp. (2.7%) *Providencia* sp. (1.4%) and *P. aeruginosa* (1.4%).

**Table 1**: Distribution of bacterial meningitis cases by age group and gender

| Age group (yr) | Total number | Male Meningitis cases | Female Meningitis cases | Male | Female |
|----------------|--------------|-----------------------|-------------------------|------|--------|
| 1month-2 Y    | 602          | 19                    | 3.16                    | 409  | 13     |
| 2-4 Year      | 319          | 17                    | 5.33                    | 188  | 10     |
| 4-6 Year      | 131          | 5                     | 3.82                    | 77   | 3      |
| 6-8 Year      | 30           | 2                     | 6.67                    | 25   | 1      |
| 8-12 Year     | 47           | 2                     | 4.25                    | 25   | 1      |
| Total         | 1129         | 45                    | 3.98                    | 724  | 28     |

**Table 2**: The isolated species from the clinical samples

| Isolated Pathogens | n | %  |
|--------------------|---|----|
| *N. meningitides*  | 35| 47.9|
| *S. pneumonia*     | 11| 15.1|
| *H. influenzae*    | 10| 13.7|
| *E. coli*          | 8 | 11.0|
| *Enterobacter* spp.| 5 | 6.8 |
| *Citrobacter* spp. | 2 | 2.7 |
| *Providencia* spp. | 1 | 1.4 |
| *Pseudomonas* aeruginosa | 1 | 1.4 |

Abbreviations. N=Neisseria, S=Streptococcus, H=Haemophilus

Available at: [http://ijph.tums.ac.ir](http://ijph.tums.ac.ir)
Table 3 illustrates the socio-demographic factors that might be contributed in developing of bacterial meningitis. The statically significance associated with developing of infection was obtained with malnutrition (low hemoglobin level) $P$-value<0.001 and high house crowdness $P$-value 0.037. Simultaneously, the risk factors were represented by Odds ratio (>1.0), malnutrition showed a risk factor for developing of bacterial meningitis Odds ratio 2.7 followed by house crowdness odds ratio 1.7 and low family income odds ratio 1.6 (Table 3).

Table 4 illustrates the direct effect of the isolated pathogens on the development of anemia while Table 5 shows the effect of the same pathogens on development of leucocytosis in infected patients; both analyses demonstrated clearly that $S.\ pneumonia$ was the significant factor in development of these pathological effects.

Table 6 illustrates the symptoms accompanied the meningitis cases, the fever was the most frequent symptom followed by neck stiffness and vomiting, other minor symptoms were poor feeding and irritability.

### Table 3: The demographic characteristics and the risk factors associated with developing of bacterial meningitis

| Variables                      | Total no cases | Meningitis cases | Percentage | $P$-value | Odds ratio | 95% C.I       |
|--------------------------------|----------------|------------------|------------|-----------|------------|--------------|
| Malnutrition/(Hemoglobin)      |                |                  |            |           |            |              |
| Yes                            | 840            | 50               | 6.0        | <0.001    | 2.62       | 1.58-4.31    |
| No                             | 1013           | 23               | 2.3        |           |            |              |
| Family income                  |                |                  |            |           |            |              |
| Low                            | 1070           | 50               | 4.7        | 0.068     | 1.59       | 0.96-2.63    |
| High Moderate                  | 783            | 23               | 2.9        |           |            |              |
| House Crowdness                |                |                  |            |           |            |              |
| Per room $\leq 3.0$            | 803            | 23               | 2.9        |           |            |              |
| $>3.0$                         | 1050           | 50               | 4.8        | 0.045     | 1.66       | 1.01-2.74    |
| Gender                         |                |                  |            |           |            |              |
| Male                           | 1129           | 43               | 3.8        | 0.728     | 0.92       | 0.57-1.48    |
| Female                         | 724            | 30               | 4.1        |           |            |              |
| Mother education               |                |                  |            |           |            |              |
| Elementary                     |                |                  |            |           |            |              |
| Secondary                      | 660            | 30               | 4.5        | 0.34      | 1.26       | 0.78-2.03    |
| University                     | 563            | 20               | 3.6        |           |            |              |
|                               | 630            | 23               | 3.7        |           |            |              |
| Other diseases/RTI             |                |                  |            |           |            |              |
| Septicemia                     | 300            | 14               | 4.7        | 0.98      | 0.99       | 0.51-1.94    |
| UTI                            | 370            | 20               | 5.4        | 0.40      | 1.32       | 0.69-2.53    |
|                               | 140            | 4                | 2.9        | 0.16      | 0.48       | 0.16-1.3     |

Abbreviations: RTI= Respiratory Tract Infection, UTI=Urinary Tract Infection; $P$-value: significant at 0.05, CI= Confidence interval

### Table 4: Pairwise comparison among differences of three pathogens in anemic patients

| Organism I | Organism J | Mean difference I-J | SE      | $P$-value |
|------------|------------|----------------------|---------|-----------|
| $N. meningitides$ | $H. influenza$ | 0.15857              | 0.32598 | 1.000     |
|             | $S. pneumonia$ | 0.79403              | 0.31367 | 0.043     |
| $H. influenza$ | $N. meningitides$ | -0.15857             | 0.32538 | 1.000     |
|             | $S. pneumonia$ | 0.63545              | 0.39649 | 0.345     |
| $S. pneumonia$ | $N. meningitides$ | -0.79403             | 0.31367 | 0.043     |
|             | $H. influenza$ | -0.635456            | 0.39649 | 0.345     |

Abbreviations: STD= Standard deviation
Table 5: Pairwise comparison among differences of three pathogens in relation to leukocytosis in CSF

| Organism I      | Organism J      | Mean difference I-J | STD Error | P value |
|-----------------|-----------------|---------------------|-----------|---------|
| N. meningitides | H. influenza    | 1904-286            | 1241.443  | 0.393   |
|                 | S. pneumonia    | -1972-987           | 1196.749  | 0.043   |
| H. influenza    | N. meningitides | -1904-286           | 1241.443  | 0.393   |
|                 | S. pneumonia    | -3877-273           | 1512.752  | 0.044   |
| S. pneumonia    | N. meningitides | 1972-987            | 1196.749  | 0.315   |
|                 |                 | 3877-273            | 1512.752  | 0.040   |

Table 6: The Clinical Symptoms associated of Bacterial meningitis

| Clinical Symptoms | n | % |
|-------------------|---|---|
| Fever             | 57| 78|
| Vomiting          | 27| 37|
| Neck stiffness    | 34| 47|
| Irritability      | 12| 16|
| Poor feeding      | 14| 19|

Discussion

An accurate laboratory confirmation of the etiology in acute bacterial meningitis (ABM) is essential to provide optimal patient therapy, appropriate case contact management, and reasoned public health actions, it also provides information upon which to base decisions regarding immunization programs, especially for countries without routine vaccination against the main acute bacterial meningitis pathogens (21, 22). The present cross sectional study showed the pattern of bacterial meningitis in children younger than twelve years of age and reported the pattern of the disease in district hospitals which may reflects the pattern of the disease in the central and north catchment areas of Gaza strip.

In our study, only 73 (4%) cases proved to contain viable bacterial pathogens out of 1853 confirmed cases by cells in according of inclusion criteria of probable ABM cases. The infection rate recorded is low in comparison to big number of suspected specimens by cells. Reasons as reviewed in other studies for low CSF culture yield are low bacterial load, use of antimicrobial agents prior to CSF collection, poor culture media (23), poor culture facility such as non-availability of special media, stored in unsatisfactory conditions, samples refrigerated before plating, delayed and faulty inoculated, lack of transport media and inadequacy in processing of CSF specimens (24), lack of 24 hours facility for processing CSF samples (25). In our study, the probable cause was the use of antibiotics prior hospitalization. It is well known that meningitis developed as a complication for initial infection like pneumonia, sepsis, and otitis. Therefore, these infections might unwell treated (26, 27). Forty five (62 %) of cases in our study were male. These results showed no sex significant difference with male infection higher than females. More infection was in the age group of 1-month-two years with frequency (44%), and 81% of confirmed bacterial meningitis belonged to age group 1-month-4 years, these age groups for the children have considered as development age and they are more susceptible to infection than elder one (28).

In diagnosis of acute bacterial meningitis, usually blood culture was carried out in parallel with CSF analysis which can be used as tool of diagnosis the bacteria has three steps to reach to the meninges, the second step is the invasion of the blood. Fifty seven percent of meningitis cases showed blood positive in our trial, also gram stain was carried out in parallel of cells excluding 12 cases which were positive only on gram-stain and not by cul-
ture. Similar results were obtained when a comparison was carried out between PCR, Gram and culture in which gram and PCR are not affected by antibiotics (29).

The main symptoms accompanied the meningitis cases were the fever followed by neck stiffness and vomiting, similar symptoms were recorded in some reports (30-32). It was noted that some cases have no fever which reflects the asymptomatic cases and this was recorded in some reports (33-35).

The latex agglutination test (LAT) was used in comparison with culture and with some CSF negative culture which contain cells >100 cells. The results showed that out of 120 cases with negative CSF culture examined 18% were positive by LAT. This test result is used to inform the pediatricians for treatment of bacterial infection. Some studies demonstrated that LAT was more sensitive compared to conventional Gram stain and culture technique in identifying the fastidious organisms like H. influenzae, S. pneumoniae and Group B Streptococcus (36).

N. meningitides is the leading cause of meningitis in our area. No previous precise information to be compared in our past data. These etiological agents and their relative frequency may vary in different geographical areas. Tzanakaki & Mastrantonio (2007) reported that the etiology of bacterial meningitis in Europe and in the Mediterranean region N. meningitidis, S. pneumoniae and H. influenzae type b were most commonly associated with bacterial meningitis accounting for almost 90% of reported cases of acute bacterial meningitis in infants and young children (5). Mani et al. reported that S. pneumoniae was the predominant pathogen accounting for 238 (61.8%) cases. Haemophilus influenzae and N. meningitidis accounted for 7 (1.8%) and 4 (1%) cases respectively in India (24). This difference in the frequencies of the causative agents may be attributed to the applying of vaccination regimen and other socioeconomically factors associated with target group of the study area. The introduction of vaccination regimen of H. influenzae and S. pneumonia and N. meningitidis in different countries induced great reduction of these pathogens from the community (37).

The risk factors associated with developing such an infection using Chi square test with P-value of <0.05 and Odds ratio with level 0>1.0 showed that there was statically significant association with the malnutrition (low hemoglobin level). These factors showed clearly that the anemic patients were highly susceptible to serious infection, and it is well known that the developing countries and Gaza strip are highly endemic with anemia with different causative agents (38, 39). Simultaneously, house crowding encouraged the development of meningitis due to most of the detected pathogens are air transmission and the smoking in these houses played an important role in diminishing the capacity of epithelial cells covering the respiratory tract for prevention of acquiring infection in addition to the prevalence of healthy carriers of pathogens (40,41).

The Anova test demonstrated that the impact effect of the presence of the three main pathogens in the blood and CSF of the children, the test proved clearly that the presence of S. pneumonia caused hemolysis of the blood causing anemia and induced the development of leukocytosis in the blood of patients.

The study had several potential limitations. First, this is a cross sectional study analyzing only notified cases of meningitis; thus the true incidence of disease in the community may have been underreported. Second, detailed information before presentation of meningitis was missing, and cases of presumed viral meningitis could have represented cases of partially treated bacterial meningitis, thus affecting the results. A final limitation of our study is our inability to follow up and record the complications including the neurological ones in the survivor of acute bacterial meningitis.

**Conclusion**

The bacterial meningitis is still predominant among the children and N. meningitides is the dominant causative agent and needs vaccination. The risk factors should be taken in consideration in any future planning.
Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgments

We thank all the Staff of Al Nassr and Al Dora pediatric hospitals for their help with the data collection, the samples collection and analysis. The authors declare that there is no conflict of interests.

References

1. World Health Organization (2003). The world health report 2003. Shaping the future. Geneva WHO.
2. Wegner JD, Hightower AW, Faeklam RR, Gaventa S, Broome CV (1990). Bacterial meningitis in United States, 1986: report of a multistate surveillance study. J Inf Dis, 162: 1316-1323.
3. Brouwer MC, van de Beek D (2012). Bacterial meningitis. Ned Tijdschr Tandheelkd. May,119(5): 238-42.
4. Lipke M, Karasek E (2013). Meningitis and encephalitis in Poland in 2011. Przegl Epidemiol, 67(2): 207-12, 327-30.
5. Tzanakaki G, Mastrantonio P (2007). Aetiology of bacterial meningitis and resistance to antibiotics of causative pathogens in Europe and in the Mediterranean region. Int J Antimicrob Agents, 29 (6): 621-9. Epub 2007 Mar 26.
6. Teleb N, Plishvili T, Van Beneden C et al. (2013). Bacterial meningitis surveillance in the Eastern Mediterranean region, 2005-2010: successes and challenges of a regional network. J Pediatr, 163 (1 Suppl): S25-31.
7. Ghotaslou R, Farajnia S, Yeganeh F, Abdoli-Oskouei S, Ahangarzadeh Rezaee M, Barzegar M (2012). Detection of acute childhood meningitis by PCR, culture and agglutination tests in Tabriz. Acta Med Iran, 50(3):192-6.
8. Mahmoudi S, Zandi H, Pourakbari B, Ashtiani MT, Mamishi (2013). Acute bacterial meningitis among children admitted into an Iranian referral children's hospital. Jpn J Infect Dis, 66(6):503-6.
9. Shaban I, Siam R (2009). Prevalence and antimicrobial resistance pattern of bacterial meningitis in Egypt. Ann Clin Microbiol Antimicrob, Sep 24; 8:26.
10. Al Khonsasi A, Banajeh (2006). Bacterial profile and clinical outcome of childhood meningitis in rural Yemen: a 2-year hospital-based study. J Infect, 53(4):228-34. Epub 2006 Jan 23.
11. Gessner BD (2009). Haemophilus influenzae type b vaccine impact in resource-poor settings in Asia and Africa. Expert Rev Vaccines,8(1):91-102.
12. Watt JP, Wolfson LJ, O'Brien KL et al. (2009). Hib and Pneumococcal Global Burden of Disease Study Team. Burden of disease caused by Haemophilus influenzae type b in children younger than 5 years: global estimates. Lancet, 12; 374(9693):903-11.
13. Chadwick DR, Lever AM (2002). The impact of new diagnostic methodologies in the management of meningitis in adults at a teaching hospital. QJM, 95:663c70.
14. Poppert S, Essig A, Stoehr B, Steingruber A, Wirths B, Juretschko S (2005). Rapid diagnosis of bacte
erial meningitis by real-time PCR and fluorescence in situ hybridization. J Clin Microbiol, 43:3390c7.
15. Ben RJ, Kung S, Chang FY, Lu JJ, Feng NH, Hsieh YD (2008). Rapid diagnosis of bacterial meningitis using a microarray. J Formos Med Assoc, 107(6): 448-53.
16. Trampaiz A, Steinhuber A, Wittwer M, Leib SL (2007). Rapid diagnosis of experimental meningitis by bacterial heat production in cerebrospinal fluid. BMC Infect Dis, 10; 7:116.
17. Lv S, Zhao J, Zhang J, Kwon S, Han M, Bian R, Fu H, Zhang Y, Pan H (2014). Tumor necrosis factor z level in cerebrospinal fluid for bacterial and aseptic meningitis: a diagnostic meta-analysis. Eur J Neurol, 21(8):1115-23.
18. Rezaei M, Mamishi S, Mahmoudi S, Pourakbari B, Khotaei G, Daneshjou K, Hashemi N (2013). Cerebrospinal fluid ferritin in children with viral and bacterial meningitis. Br J Biomed Sci, 70(3):101-3.
19. Segawa S, Sawai S, Murata S, Nishimura M, Beppu M, Sogawa K, Watanebe M, Satoh M, Matsutani T, Kobayashi M, Iwadate Y, Kuwabara S, Saeki N, Nomura F (2014). Direct application of MALDI-TOF mass spectrometry to cerebrospinal fluid for rapid pathogen identification in a patient with bacterial meningitis. Clin Chim Acta, 4. pii: S0009-8981(14)00191-0.
20. World Health Organization (1996). Vaccine research and development: Generic protocol for population-based surveillance of Haemophilus influenzae type B, Geneva.

Available at: http://ijph.tums.ac.ir
21. Lukšić I, Mulič R, Falconer R, Orban M, Sidhu S, Rudan I (2013). Estimating global and regional morbidity from acute bacterial meningitis in children: assessment of the evidence. *Croat Med J*, 54(6):510-8.

22. Greenhow TL, Hung YY, Herz AM, Losada E, Pantell RH (2014). The changing epidemiology of serious bacterial infections in young infants. *Pediatr Infect Dis J*, 33(6):595-9.

23. Martin NG, Sadarangani M, Pollard AJ, Goldacre MJ (2014). Hospital admission rates for meningitis and septicaemia caused by *Haemophilus influenzae*, *Neisseria meningitidis*, and *Streptococcus pneumoniae* in children in England over five decades: a population-based observational study. *Lancet Infect Dis*, 14(5):397-405.

24. Mari R, Pradhan S, Nagarathna S, Wasiulla R, Chandramukhi A (2007). Bacteriological profile of community acquired acute bacterial meningitis: A ten-year retrospective study in a tertiary neuro-care centre in South India. *Indian J Med Microbiol*, 25:108–14.

25. Sahai S, Mahadevan S, Srinivasan S, Kanungo R (2001). Childhood bacterial meningitis in Pondicherry, South India. *Indian J Pediatr*, 68:839.

26. Heckenberg SG, Brouwer MC, van de Beek D (2014). Bacterial meningitis. *Handb Clin Neurol*, 121:1361-75.

27. Vo-Tan D¹, Portmann D, Carrat X (2010). From barotrauma otitis to a fulminant meningitis. *Rev Laryngol Otol Rhinol (Bord)*, 131(3):229-32.

28. Swann O¹, Everett DB, Furry J, Harrison EM, Msukwa MT, Heyderman RS, Molyneux EM (2014). Bacterial meningitis in Malawian infants <2 months of age: etiology and susceptibility to world health organization first-line antibiotics. *Pediatr Infect Dis J*, 33(6):560-5.

29. Wu HM, Cordeiro SM, Harcourt BH et al. (2013). Accuracy of real-time PCR, Gram stain and culture for *Streptococcus pneumoniae, Neisseria meningitidis* and *Haemophilus influenzae* meningitis diagnosis. *BMC Infect Dis*, 22, 13:26.

30. Jugararu G, Miftode E, Teodor D, Lea D, Dorobat CM (2012). Clinical features and course of bacterial meningitis in children. *Rev Med Chir Soc Med Nat Iasi*, 116(3):722-6.

31. Fouad R, Khairy M, Fathalah W et al. Role of Clinical Presentations and Routine CSF Analysis in the Rapid Diagnosis of Acute Bacterial Meningi-

tis in Cases of Negative Gram Stained Smears. *J Trop Med*, 2014;213762. doi: 10.1155/2014/213762.

32. Carbonnelle E (2009). Laboratory diagnosis of bacterial meningitis: usefulness of various tests for the determination of the etiological agent. *Med Mal Infect*, 39(7-8):581-605.

33. Abe KA, Ishiwada N, Hoshino T, Kohno Y (2007). Two cases of meningitis caused by the same *Haemophilus influenzae* type B strain in a nursery at a 3-month interval. *Kansenshogaku Zasshi*, 81(1):72-5.

34. Fukushima K, Noda M, Saito Y, Ikeda T (2012). *Streptococcus suis* meningitis: report of a case and review of the literature. *Intern*, 51(21):3073-6. Epub 2012 Nov 1.

35. Perera N, Abulhoul L, Green MR, Swann RA (2005). Group A streptococcal meningitis: case report and review of the literature. *J Infect*, 52(2):E1-4.

36. Mohammadi SF, Patil AB, Nadagir SD, Nandihal N, Lakshminarayana SA (2013). Diagnostic value of latex agglutination test in diagnosis of acute bacterial meningitis. *Ann Indian Acad Neurol*, 16(4):645-9.

37. Martin NG, Sadarangani M, Pollard AJ, Goldacre MJ (2014). Hospital admission rates for meningitis and septicaemia caused by *Haemophilus influenzae*, *Neisseria meningitidis*, and *Streptococcus pneumoniae* in children in England over five decades: a population-based observational study. *Lancet Infect Dis*, 14(5):397-405.

38. Sirdah MM, Yaghi A, Yaghi AR (2014). Iron deficiency anemia among kindergarten children living in the marginalized areas of Gaza Strip, Palestine. *Rev Bras Hematol Hemoter*, 36(2):132-8.

39. Shubair ME (2014). Comments on: iron deficiency anemia among kindergarten children living in the marginalized areas of Gaza Strip, Palestine. *Rev Bras Hematol Hemoter*, 36(2):104-5.

40. Li MS, Wang M, Fu ZY (2010). Pathogenesis surveillance of epidemic cerebrospinal meningitis in Shandong Province in 2007/2008. *Zhongguo Yi Xue Hui Xue Yu Yi Chao*, 16(1):44-6.

41. Boué S, De Léon H, Schlage WK et al. (2013). Cigarette smoke induces molecular responses in respiratory tissues of ApoE(-/-) mice that are progressively deactivated upon cessation. *Toxicology*, 6; 314(1):112-24.