



Original Article

Evaluation of the Laboratory, Epidemiological and Clinical Characteristics of Meningitis Patients Admitted to the Hospitals of Yazd from 2009 to 2013

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ABSTRACT

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Key words

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Background and Aims: Since the epidemiological, clinical and experimental characteristics of meningitis are different for various locations, this study was conducted to investigate the characteristics of meningitis patients admitted to hospitals of Yazd in the 2009 to 2013.

Materials and Methods: In this cross-sectional and descriptive study, all 261 patients with meningitis were considered in Yazd hospitals in the years 2009 to 2013. The type of sampling method was census. The data were collected from patients' files using special forms that were designed for this purpose.

Results: In this study, 158 men (60.5%) and 103 women (39.5%) were considered. Among the patients, 53 people (20.30%) were under one-year-old, 63 people (24.14%) were between one to seven-year-old, and 85 people (32.57%) were adult. Among 261 patients, 126 ones (48.28%) and 135 ones (51.72%) were hospitalized with a diagnosis of non-bacterial meningitis and bacterial meningitis respectively. Generally, the cultivations of just 4 people (1.5%) were positive. The percentage of neutrophils and lymphocytes, the amount of glucose and the protein of cerebrospinal fluid in bacterial and aseptic meningitis was significantly different ($p < 0.001$), but the total number of white blood cells, red blood cells and lactate dehydrogenase levels were not significantly different between the two groups.

Conclusions: Since there is no significant difference between epidemiological characteristics and clinical symptoms in bacterial and no-bacterial meningitis, it seems that doing laboratory tests, despite aggressive, is the best practice for differentiating between types of meningitis and the fast performance of it could somewhat prevent the improper antibiotic therapy.

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Introduction

Meningitis is an infectious disease caused by viral, bacterial (*Haemophilus Influenza*, *Meningococcus*, etc.) factors or other microbes that is caused the inflammatory leptomeninges response, and it could be diagnosed by abnormal number of white blood cells, as well as the changes in cerebrospinal fluid (CSF) glucose and protein [1]. The disease can endanger the patient's life due to the proximity of inflammation to the brain and spinal cord. Therefore, this disease is classified as a medical emergency [2, 3]. Meningitis is an important health problem and if it is not diagnosed in the early stages and treated immediately, it has high mortality rate and complications [3]. There are an estimated 1.2 million cases of bacterial meningitis worldwide each year [4] resulting in 180,000 deaths among children aged 1–59 months. The global picture of disease indicate seasonal variation with case-fatality rates of 30% and 7% in higher-income countries [5, 6]. In recent years, incidence of bacterial meningitis has decreased in developed countries due to massive vaccination against *Haemophilus Influenza*. Although, the development of bacterial meningitis continues in developing countries [7].

Majority of the patients who are hospitalized with suspected meningitis actually are not infected with bacterial meningitis. However, routine antibiotic therapy is performed for the patients that would cause problems such as the incidence of drug-resistant bacteria, as well as false negative results for the tests [8, 9]. While, performing laboratory and clinical tests

such as Lumbar Puncture (LP) and blood tests could help the early diagnosis of the disease. One of the problems related to the patients that are infected with meningitis is consumption of antibiotics before doing LP, which in some cases leads to negative cultivation of cerebrospinal fluid for the patients infected with bacterial meningitis (partially treated meningitis), and it confuses the doctors in visiting patients [10, 11]. Although this problem has been solved to some extent in the developed countries using diagnostic procedures such as latex agglutination, antigen detection and polymerase chain reaction, in countries where financial and technology resources are limited, it would create trouble in diagnosis and treatment [12]. Meningitis cannot usually be diagnosed based on symptoms alone because the most meningitis have the common symptoms of fever, convulsions and vomiting. CSF analysis and culture is the most appropriate sample for diagnosis [13, 14]. Pathological decrease of the CSF/serum glucose ratio or increased lactate concentration indicates bacterial or fungal meningitis or leptomeningeal metastases. Elevated albumin CSF/serum ratio is a non-specific finding, but occurs mainly in bacterial [15].

The published studies about these variables in different regions of the world lead to different and sometimes conflicting results, and using these features to differentiate bacterial meningitis from non-bacterial has been challenged [16]. In Iran, *Haemophilus*

Influenza and *Strep. pneumoniae* is the most common cause of bacterial meningitis in children under 5 years old, respectively [17].

Because of the high prevalence of meningitis in Iran, as well as different outbreaks, clinical and laboratory characteristics in different regions and the fact that we have not found a study on the subject in Yazd recently, we decided to do the present study to evaluate laboratory, epidemiological and clinical characteristics of meningitis patients in the hospitals of Yazd from 2009 to 2013.

Materials and Methods

This is a descriptive study that was performed with the cross-sectional and retrospective method. It was performed on 261 patients who were admitted to the 7 hospitals in Yazd city (Shahid Sadoughi, Shahid Rahnemoun, Afshar, Shohaday e Kargar, Seid o Shohada, Mojibian, Goudarz) from 2009 to 2013. Inclusion criteria included all the patients that were hospitalized based on clinical symptoms, physical examination and analysis of cerebrospinal fluid in these years. Inappropriate CSF sample and incomplete records were excluded.

The required data were collected from the patients' medical files using special forms that were designed for this purpose. This form consists of two parts: the first part includes personal information such as age, sex, date of onset of symptoms, date of diagnosis, initial symptoms of patients when admitted to the hospital, and the final diagnosis of meningitis. The second part included laboratory criteria for analyzing cerebrospinal fluid including cultures, white and red blood cell count, the

amount of protein, levels of lactate dehydrogenase, the amount of glucose, levels of lymphocytes and neutrophils. Subsequently, the collected data were analyzed using the SPSS16 software. The chi-square test and T-test have been used for comparison, and the p-value was reported.

Results

The number of 261 patients diagnosed with meningitis has been admitted in hospitals of Yazd during the years 2009 to 2013. Fig. 1 represents the frequency distribution of the final diagnosis of meningitis in the patients suffering from bacterial and non-bacterial meningitis.

158 (60.5%) of the patients were men, and 103 (39.5%) of the patients were women. The ratio of male to female was 1.54 to 1. The final diagnosis of 126 patients (48.28%) was non-bacterial meningitis and 135 cases (51.72%) was bacterial meningitis. As we can see from table 1, the age and sex distribution of the patients in two types of meningitis had no significant difference, but most cases admitted in the spring (70%) was non-bacterial meningitis, and most cases admitted in the winter (77.6%) was bacterial meningitis ($p < 0.001$). The distribution of the clinical symptoms for two types of bacterial and non-bacterial meningitis is listed in table 2. The most common symptoms in both groups were fever, vomiting and nausea. Only the frequency of fever was significantly higher in bacterial meningitis (0.034), in general, the frequency of other symptoms ($p < 0.05$) and the total frequency of clinical symptoms were not significantly different for both of the groups ($p = 0.588$).

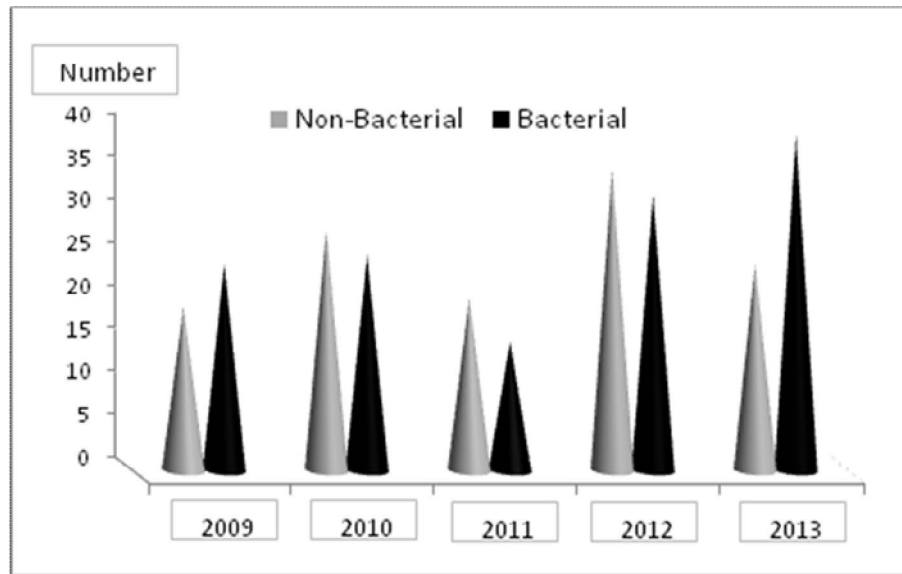


Fig. 1. Distribution of final diagnosis of meningitis based on the year of diagnosis.

Table 1. The comparison of epidemiologic characteristics of the patients according to the types of meningitis.

		Non-bacterial meningitis (N=126) Number (%)	Bacterial meningitis (N=135) Number (%)	Total (N=261) Number (%)	P- value
Sex	Male	77 (48.7)	81 (51.3)	158 (100)	0.854
	Female	49 (47.6)	54 (52.4)	103 (100)	
Age (Year)	< 1	25 (47.2)	28 (52.8)	53 (100)	0.136
	1-7	24 (38.1)	39 (61.9)	63 (100)	
	8-18	36 (60)	24 (40)	60 (100)	
	>= 19	41 (48)	44 (52)	85 (100)	
Season	Spring	56 (70)	24 (30)	80 (100)	0.001
	Summer	36 (58.1)	26 (41.09)	62 (100)	
	Autumn	19 (36.5)	33 (63.5)	52 (100)	
	Winter	15 (22.4)	52 (77.6)	67 (100)	

Table 2. Comparison the presence of clinical symptoms according to the final diagnosis of meningitis.

Clinical symptoms	Non-bacterial meningitis (N=126) Number (%)	Bacterial meningitis (N=135) Number (%)	Total (N=261) Number (%)	P- value
Fever	105 (83.3)	125 (92.6)	230 (88.1)	0.034
Vomit	60 (47.6)	49 (36.3)	109 (41.8)	0.084
Nausea	45 (35.7)	35 (25.9)	80 (30.6)	0.114
Headache	39 (31.01)	32 (23.7)	71 (27.2)	0.239
Poor feeding	19 (15.1)	24 (17.8)	43 (16.5)	0.478*
Lethargy	15 (11.9)	19 (14.1)	34 (13.0)	0.757*
Restlessness	11 (8.7)	12 (8.9)	23 (8.8)	0.397*
Convulsion	7 (5.6)	7 (5.2)	14 (5.4)	0.887
Cough	2 (1.6)	4 (3.0)	6 (2.3)	0.743

*The frequency of poor feeding, lethargy and restlessness were tested among infants under one year old.

The investigation of the results of cultivation of cerebrospinal fluid showed that four (1.5%) of the patients with a diagnosis of meningitis have positive cultivation of cerebrospinal fluid. The results of the positive cultivations had been one case of *Enterovirus*, one case of *Streptococcus*, one case of *E.coli* and one case of *Neisseria*. Table 3 represents laboratory characteristics of cerebrospinal fluid in both of the bacterial meningitis and non-bacterial

meningitis groups. The percentage of neutrophils and lymphocytes, the amount of glucose and cerebrospinal fluid protein in bacterial and nonbacterial meningitis were significantly different ($p<0.001$). However, the total count of white blood cells, red blood cells and lactate dehydrogenase (LDH) levels were not significantly different between the two groups (see Table 3).

Table 3. Comparison of laboratory parameters of cerebrospinal fluid according to the final diagnosis of meningitis.

	Non-bacterial meningitis (N=126)	Bacterial meningitis (N=135)	P-value
White blood cell count (number/ml)	308±803	440±1091	0.269
Red blood cell count (number/ml)	96±373	207±1929	0.526
Lymphocyte count (number/ml)	72±21	27±20	0.001
Neutrophil count (number/ml)	25±21	70±21	0.001
Glucose (mg/dL)	63±22	32±18	0.001
Protein content (mg/dL)	36±22	68±28	0.001
The amount of LDH (mg/dL)	56±60	61±60	0.459

The data are presented as Mean±SD

Discussion

Review of the data shows that the number of people suffering from bacterial meningitis was higher than the number of patients with non-bacterial meningitis. viral meningitis is more common in western countries [9] and according to other studies, viral meningitis is more than bacterial, that does not match with our findings [18]. Diagnosis based on CSF changes no culture results, lack of laboratory equipment for viral infection diagnosis in many hospitals and inappropriate sampling may be reasons for this difference. Patients with viral meningitis not admitted in hospitals due to the milder symptoms, so it is other reason that viral meningitis, which is usually

self-limited [19] and less common in hospitalized patients [14].

In this study, the value of cultures to confirm the diagnosis of meningitis was very weak because only 1.5% of patients had positive culture that has not matched with others studies that cultures were positive in 50 to 80% of patients [20]. Comparison of the results suggests that antibiotic therapy during visiting by several doctors before a final diagnosis or accuracy of laboratory devices may lead to the obvious differences in the results. It is also in similar studies in Iran [14, 18, 21]. In the evaluation of cerebrospinal fluid leukocytes, we came to the conclusion

that this variable has high diagnostic value, and this value increases with age such that leukocytes was increased by 100% for the age group of above 7 years. This result is the same for both of the bacterial and non-bacterial meningitis. The studies also show an increased neutrophil in bacterial meningitis, and we have observed an increased lymphocyte for non-bacterial meningitis. There is a significant relationship between the increase in the neutrophil and final bacterial diagnosis [22]. The average amount of neutrophil was 70 ± 21 in bacterial meningitis, and the average amount of lymphocytes was 72 ± 21 in non-bacterial meningitis. We also concluded that there is a significant relationship between increased lymphocytes and non-bacterial meningitis, which was consistent with the most of previous publications.

The study also found that there was a significant relationship between the number of neutrophils, lymphocytes, white blood cells, the amount of protein and glucose with a final diagnosis. It is consistent with the results of other researchers and confirm the use of typical criteria for differential diagnostic approach [23]. Evaluating the results, we found that meningitis have been seen more frequently in males than in females, which are consistent with the published articles [18, 21, 24]. In our study, the highest prevalence was at ages under 7 years (44.4%), that are consistent with other studies that is due to raising of human immunity by age increasing [25] and no routine vaccination of children for meningitis prevention in Iran during this survey, fortunately Hib vaccine added to

vaccination program of children recently and has remarkably reduced Hib meningitis in Iran [13]. In reviewing clinical symptoms, the fever was the most common patient complaints, generally. After fever, vomiting, nausea and convulsions were the most common patient complaint, respectively. Also, at lower ages, poor feeding and lethargy were the top causes of the patient's visit after fever that is similar to other studies. These finding are not helpful for differential diagnosis of bacterial and non-bacterial meningitis although fever is significantly more common in bacterial type, but it cannot specific [7, 26-28]. Incomplete hospital records and ignoring physical examination findings with low confirmed etiologic cause were the most obvious limitation of our study, but high hospital records coverage (Lack of cooperation of one hospital, only) and 5 years data analysis are the strength of this survey.

Conclusions

Since there is no significant difference between epidemiological characteristics and clinical symptoms of bacterial and non-bacterial meningitis, it seems that laboratory tests, despite aggressiveness, is the best practice to differentiate different types of meningitis, and the fast performing of it could prevent inappropriate antibiotic therapy. For better diagnosis, proposed Hospitals are equipped to detect viral infections, as well as increasing awareness of physician about rational use of antibiotics to prevent misdiagnosis.

Conflicts of Interest

The authors have no conflicts of interest to declare.

Acknowledgments

There is no acknowledgement to declare.

References

- [1]. Dery M, Hasbun R. Changing epidemiology of bacterial meningitis. *Curr Infect Dis Rep*. 2007; 9(4): 301-7.
- [2]. Karanika M, Vasilopoulou VA, Katsioulis AT, Papastergiou P, Theodoridou MN, Hadjichristodoulou CS. Diagnostic Clinical and Laboratory Findings in Response to Predetermining Bacterial Pathogen: Data from the Meningitis Registry. *PloS one* 2009; 4(7): e6426.
- [3]. Abdinia B, Rezaee MA, Oskouie SA. Etiology and Antimicrobial Resistance Patterns of Acute Bacterial Meningitis in Children: A 10-Year Referral Hospital-Based Study in Northwest Iran. *Iranian Red Crescent Medical Journal* 2014; 16(7).
- [4]. Heydari B, Khalili H, Karimzadeh I, Emadi-Koochak H. Clinical, Paraclinical, and Antimicrobial Resistance Features of Community-Acquired Acute Bacterial Meningitis at a Large Infectious Diseases Ward in Tehran, Iran. *Iranian Journal of Pharmaceutical Research* 2016; 15(1): 347-54.
- [5]. Mosavi-Jarrahi A, Esteghamati A, Asgari F, Heidarnia M, Mousavi-Jarrahi Y, Goya M. Temporal analysis of the incidence of meningitis in the Tehran metropolitan area, 1999-2005. *Population Health Metrics* 2009; 7(1): 1-7.
- [6]. van de Beek D. Progress and challenges in bacterial meningitis. *Lancet* (London, England). 2012; 380(9854): 1623-624.
- [7]. Tunkel AR, Scheld W. Acute meningitis. *Principles and practice of infectious diseases*. 2000; 5: 959-97.
- [8]. Welinder-Olsson C, Floren-Johansson K, Larsson L, Oberg S, Karlsson L, Ahren C. Infection with Pantón-Valentine leukocidin-positive methicillin-resistant *Staphylococcus aureus* t034 a. *Emerg Infect Dis*. 2008; 14(8): 1271-2.
- [9]. Kyaw M, Lynfield R, Schaffner W, Craig A, Hadler J, Reingold A, et al. Effect of introduction of the pneumococcal conjugate vaccine on drug-resistant *Streptococcus pneumoniae*. *N Engl J Med*. 2006; 354(14): 1455.
- [10]. Duan QJ, Shang SQ, Wu YD. Rapid diagnosis of bacterial meningitis in children with fluorescence quantitative polymerase chain reaction amplification in the bacterial 16S rRNA gene. *Eur J Pediatr*. 2009; 168(2): 211-16.
- [11]. Husain EH, Bahbahani E, Al-Shawaf F, El-Nabi MH, Shafiq MH, Al-Ateeqi N, et al. Aseptic meningitis among children in Kuwait. *Med Prin Pract*. 2008; 17(2): 122-25.
- [12]. Nigrovic LE, Kuppermann N, Macias CG, Cannavino CR, Moro-Sutherland DM, Schremmer RD, et al. Clinical prediction rule for identifying children with cerebrospinal fluid pleocytosis at very low risk of bacterial meningitis. *Jama-J Am Med Assoc*. 2007; 297(1): 52-60.
- [13]. Amin M, Ghaderpanah M, Navidifar T. Detection of *Haemophilus influenzae* type b, *Streptococcus agalactiae*, *Streptococcus pneumoniae* and *Neisseria meningitidis* in CSF specimens of children suspicious of Meningitis in Ahvaz, Iran. *Kaohsiung J Med Sci*. 2016; 32(10): 501-506.
- [14]. Alavi S, Moshiri N, Shokri S. Evaluation of epidemiological, clinical and laboratory findings of admitted patients with meningitis in infectious diseases ward of Razi Hospital, Ahvaz. *Scientific Medical Journal (AJUMS)*. 2010; 9(3): 221-31.
- [15]. Deisenhammer F, Bartosb A, Egga R, Gilhusc N, Giovannonid G, Rauere S, et al. Guidelines on routine cerebrospinal fluid analysis. Report from an EFNS task force. *Eur J Neurol*. 2006; 13(9): 913-22.
- [16]. van de Beek D, de Gans J, Spanjaard L, Weisfelt M, Reitsma J, Vermeulen M. Clinical features and prognostic factors in adults with bacterial meningitis. *The New England journal of medicine* 2004;351(18):1849.
- [17]. Ghotaslou R, Yeganeh-Sefidan F, Salahi-Eshlaqi B, Ebrahimzadeh-Leylabadlo H. Etiology of Acute Bacterial Meningitis in Iran: a Systematic Review. *Acta Med Iran*. 2015; 53(8): 454-61.
- [18]. Sharifi-Mood B, Khajeh A, Metanat M, Rasouli A. Epidemiology of Meningitis Studied at a University Hospital in Zahedan, South-Eastern Iran. *International Journal of Infection* 2015; 2(2).
- [19]. Mentis A-F, Kyprianou M, Xirogianni A, Kesanopoulos K, Tzanakaki G. Neutrophil-to-lymphocyte ratio in the differential diagnosis of acute bacterial meningitis. *Eur J Clin Microbiol*. 2016; 35(3): 397-403.

- [20]. Brouwer M, Tunkel A, van de Beek D. Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis. *Clin Microbiol Rev.* 2010; 23(3): 467-92.
- [21]. Kanani S, Moradi G. Epidemiological survey of acute meningitis in Kurdistan province from 1381 to the end of 1383. *Scientific Journal of Kurdistan University of Medical Sciences* 2005; 10(2): 49-54.
- [22]. Fitzwater SP, Ramachandran P, Nedunchelian K, Kahn G, Santosham M, Chandran A. Bacterial Meningitis in Children <2 Years of Age in a Tertiary Care Hospital in South India: An Assessment of Clinical and Laboratory Features. *J pediatr.* 2013;163(1): S32-S7.
- [23]. Cunha BA. The clinical and laboratory diagnosis of acute meningitis and acute encephalitis. *Expert Opin Med Diagn.* 2013; 7(4): 343-64.
- [24]. Logan S, MacMahon E. Viral meningitis. *BMJ (Clinical research ed).* 2008; 336(7634): 36-40.
- [25]. Simon AK, Hollander GA, McMichael A. Evolution of the immune system in humans from infancy to old age. *Proc Biol Sci.* 2015; 282(1821): 20143085.
- [26]. Nigrovic L, Kuppermann N, Malley R. Development and validation of a multivariable predictive model to distinguish bacterial from aseptic meningitis in children in the post-Haemophilus influenzae era. *Pediatrics* 2002; 110(4): 712-19.
- [27]. Theodoridou MN, Vasilopoulou VA, Atsali EE, Pangalis AM, Mostrou GJ, Syriopoulou VP, 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(1): 1-12.
- [28]. Husain E, Bahbahani E, Al-Shawaf F, El-Nabi M, Shafiq M, Al-Ateeqi N, et al. Aseptic meningitis among children in Kuwait. *Med Princ Pract.* 2008; 17(2): 122-25.