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Original Article

Health Management and Policy Section

Types, Risk Factors, Clinical symptoms and Diagnostic Tests of Acute Adult Meningitis in Northern Iran During 2006-2012

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ABSTRACT

Background: Acute bacterial meningitis is a medical emergency condition that requires prompt diagnosis and treatment and otherwise associated with serious morbidity and mortality.

Aim: The aim of this study was to assess types, risk factors, clinical symptoms and diagnostic tests of meningitis in hospitalized patients of Mazandaran University of medical sciences hospitals during 2006-2012.

Matherials and Methods: This is a retrospective descriptive study. Following approval of the ethics committee of Mazandaran University of Medical Sciences, records of adult patients diagnosed with acute meningitis from 2006 to 2012 were extracted from Mazandaran Provincial Health Center and patients attending hospitals affiliated to Mazandaran University of Medical Sciences.

Statistical analysis: Data were analyzed with SPSS-16 using descriptive statistics (frequency, mean, standard deviation, and median).

Results: In this study, of the 137 patients with meningitis, 73 (53.9%) were viral, 61 (46%) bacterial, 1 (0.7%) fungal, and 2 (1.4%) unknown. The majority of risk factors in patients were head trauma, upper respiratory infection, and drug addiction. The most common clinical signs were headache, fever, nausea and vomiting, and stiff neck.

Conclusion: In this study, the incidence of meningitis was much lower than any other country. It could be due to geographic variation or incomplete recording of patient's data. It is recommended to perform a longitudinal study during the coming years on patients with meningitis.

Keywords: Cerebrospinal fluid culture, Healthcare providers, Medical emergency

INTRODUCTION

Meningitis is the inflammation of leptomeningeal membranes, and is divided into septic and aseptic groups. Septic meningitis is caused by bacteria and includes acute and chronic varieties. Acute bacterial meningitis is the purulent infection of CNS, and *Streptococcus pneumonaie* is the most common causing agent, especially in people older than 50 years of age [1]. Other types of micro-organisms include *Neisseria meningitides*, Beta-*streptococcus* group, and *Haemophilus influenza* [2]. Chronic bacterial meningitis is another bacterial form of meningitis that occurs with clinical and inflammatory CSF symptoms for four weeks or longer [1]. Aseptic meningitis is caused by viral or non-viral agents with similar clinical signs and inflammatory responses. This type of meningitis has acute and subacute forms, which are categorized according to duration of disease and cellular responses in CSF. Most cases of aseptic meningitis are caused by viruses, especially Enteroviruses [1].

Studies report the incidence rate of 1.1 cases per 100,000 patients in America [3]. In another study in Paris, the prevalence of pneumococcal meningitis in ICU was 1.5% [4]. The results of a study in Italy revealed the prevalence of bacterial meningitis 3.7 per 100,000 cases [5]. In a study conducted in Firoozgar Hospital, Iran, the frequency of bacterial meningitis following craniotomy was reported 4.7% [6]. In another study conducted in Iran, the frequency of meningitis in Kurdistan Province was reported 3.13% to 5% per 1000 population [7]. Based on review of available literature, there are several risk factors associated with meningitis such as age, gender [8], otitis or sinusitis [4, 9, 10], neurosurgery [7], alcoholism, diabetes mellitus, pneumonaie, splenectomy, renal failure, chronic hepatitis with cirrhosis, endocarditis [9], cerebrospinal fluid (CSF) rhinorrhea [11], dural fistulas [4], head trauma [7], and impaired consciousness [12,13].

The classic triad signs of meningitis include fever, headache, and neck stiffness [2]. Drowsiness, nausea and vomiting, increased ICP [2], positive Kernig's signs, positive Brodzinski signs [14], photophobia [13], myalgia, seizure, cerebral oedema [15], and hydrocephalus [15], and hearing, motor and behavioral impairments [4] were reported among other signs of this disease. Meningitis is diagnosed in different ways such as cell count, smear, culture and analysis of protein and CSF sugar, blood culture, skin biopsy, urinary antigen test, PCR, serum inflammatory markers [11] and latex particle agglutination [9]. However, cerebrospinal fluid culture is the gold standard for diagnosis of meningitis [2].

Acute meningitis is a medical emergency that requires immediate diagnostic and treatment procedures, otherwise it will have serious subsequent complications such as mental disorders, reduced psychomotor function, reduced sight, seizures, reduced hearing, and impaired walking. According to available databases, no epidemiological study has been published on this disease in Mazandaran Province, so it was decided to design a study on types, risk factors, clinical symptoms and diagnostic tests of acute adult meningitis in patients admitted to hospitals affiliated to Mazandaran University of Medical Sciences from 2006 to 2012, in order to raise awareness of healthcare providers, and to provide the context for preventive actions.

MATERIALS AND METHODS

This is a retrospective descriptive study using existing data. Following approval of the ethics committee of Mazandaran University of Medical Sciences, records of adult patients diagnosed with acute meningitis from 2006 to 2012 were extracted from Mazandaran Provincial Health Center and patients attending hospitals affiliated to Mazandaran University of Medical Sciences. Inclusion criteria included all patients over 14 years of age, whose meningitis had been confirmed by performing lumbar puncture [8]. Exclusion criteria included systemic diseases such as cancers, vascular collagen diseases, and AIDS which affect clinical symptoms and CSF analysis. Patient details were recorded using demographic

questionnaire and medical findings. Variables studied included age, gender, season, place of residence, diagnosis year, antibiotics received before LP, hospital mortality rate meningitis type (bacterial, viral, fungal, and unknown), risk, clinical signs, brain disorders and diagnostic signs. In this study, data were collected by researcher and type of meningitis was determined using laboratory results by an infectious disease specialist. Validity of the questionnaire and the list that was prepared following review of literature was confirmed by five experts from university faculty members (three infectious disease specialist and two Ph.D in nursing). After completion of forms, data were analyzed with SPSS-16 using descriptive statistics (frequency, mean, standard deviation, and median).

RESULTS

In this study, 137 patients diagnosed with acute meningitis, hospitalized from 2006 to 2012 were investigated. Given the population of the province in this period, the frequency of meningitis in Mazandaran varied from 0.13% to 0.97% per 1000, of whom 28.5% were women and 71.5% were men. Mean and standard deviation of age at diagnosis was 34.35±18.28 years, with the youngest and the oldest patients as 14 years and 85 years, respectively. Most cases were reported in fall (27.6%) and summer (25.4%) in cities of Amol (31.6%) and Sari (26.5%) and in 2008 (0.97%). Of the 137 patients with meningitis, 73 (53.9%) were viral, 61 (46%) bacterial, 1 (0.7%) fungal, and 2 (1.4%) unknown. Types of bacteria identified in CSF analysis included *Streptoccocus pneumonaiee, Meningococcus, Staphylococcus*, and *Neisseria meningitidis*.

The majority of risk factors in patients were head trauma, upper respiratory infection, and drug addiction. Other risk factors included craniotomy, impaired renal function, and diabetes. The most common clinical signs were headache, fever, nausea and vomiting and stiff neck. Headache with fever and stiff neck were observed in 16.7% of cases. Other signs included reduced loss of consciousness, photophobia and positive Kernig and Brodzinski signs [Table/Fig-1].

CSF appeared clear in 43.1% of patients, turbid in 31.4%, bloody in 4.4% and unknown in 31.1%. CSF culture was reported positive only in 10.3% of cases. Details of patients' cerebrospinal fluid analysis are presented in [Table/Fig-2]. In this study, most common drug regimen included Ceftriaxone and Vancomycin (60.8%). Results showed hospital mortality rate of 8.8%.

Variable Result	YES	NO
Risk factors	**Frequency (%)**	
Head trauma	9(6.6%)	59(37%)
Upper respiratory infection	7(5.1%)	60(43.8%)
Drug addiction	8(5.8%)	61(44.5%)
Craniotomy	3(2.2%)	66(47.4%)
Impaired renal	5(3.6%)	63(46%)
Function diabetes.	2(1.4%)	66(48.2%)
Clinical signs	**Frequency (%)**	
Headache	55(40.1%)	13(9.5%)
fever	51(37.2%)	13(9.5%)
Nausea and vomiting	45(32.8%)	23(16.8%)
Stiff neck	27(19.7%)	41(29.9%)
Loss of consciousness	21(15.3%)	46(33.6%)
Photophobia	4(2.9%)	64(46.7%)
Positive Kernig signs	7(5.1%)	61(44.5%)
Positive Brodzinski signs	5(3.6%)	63(46%)

[Table/Fig-1]: Frequency and percentage of risk factors and clinical symptoms in acute adult meningitis in Mazandaran during 2006-2012

Laboratory findings (n=137)	
CSF appeared	**Frequency (%)**
Clear	59(43.1%)
Turbid	63(31.4%,)
Bloody	6(4.4%)
Unknown	29(31.1%)
Positive CSF culture	**14(10.3%)**
Streptoccocus pneumonaie	7(5.2%)
Meningococcus	5(3.7%)
Staphylococcus	1(0.7%)
Neisseria meningitidis	1(0.7%)
Negative	**64(46.7%)**
Incomplete (do not)	59(43%)
bacterial CSF	**Median (Mini-max)**
Leukocyte (cell count)	771000 (0.0-320000)
Lymphocytes (%)	20(1-94)
polymorphonuclear (%)	80(0-96)
Sugar (mg/dl)	50(5-174)
Proteins (mg/dl)	1.02(14-765)
Viral CSF	**Median (Mini-max)**
Leukocyte (cell count)	137000(0.0-30000)
Lymphocytes (%)	61.5(0-100)
polymorphonuclear (%)	23.5(0-91)
Sugar (mg/dl)	65(2-175)
Proteins (mg/dl)	49(4-1210)

[Table/Fig-2]: Laboratory findings inpatients withacutebacterial meningitisin acute adult meningitis in Mazandaran during 2006-2012

DISCUSSION

Based on population of Mazandaran Province during 2006-2012 and the present study results, the frequency of meningitis in this province varied from 0.13% to 0.97% per 1000. In a study, meningitis incidence rate in America was 1.1 cases per 100,000 patients [3]. Results of a study in Italy revealed prevalence of bacterial meningitis 3.7 per 100,000 [5]. The difference between the present study results and those of these studies may be due to geographical differences or missed diagnosis. Additionally in a study in Kurdistan, this rate was reported 3.13% to 5% per 1000 during 2002-2004 [7]. In this study, all age groups were investigated, and most cases were reported in 0 to 4 year-old age group, which may explain the difference with present study results. Findings of some studies in Iran and similar demographic region are summarized in [Table/Fig-3].

In the present study, most cases of meningitis were observed in men (71.5%) with the male:female ratio of 3:1. In most studies, gender ratio revealed higher frequency of meningitis among men. Studies conducted in Iran also confirm these results; 1.43 times in Tehran province [13], 1.83 times in Kurdistan province [7], and 3 times in Tehran province [8]. However, in a study by Kastenbauer et al., in Germany, this ratio was reported 0.9 [9], which indicate greater frequency among women, which can be due to the effect of geographical differences on gender ratio on incidence of meningitis. In terms of age, most incidences were observed in adolescence (34.35±18.28), which agrees with Abdi Liaei et al., study [8]. Similarly, in Shokouhi et al., study, mean and standard deviation of age of patients with meningitis were reported 33.5±17.8 years [15]. In Alavi et al., study, the highest frequency of meningitis was reported in the 20 to 40 year-old age group [12]. All these studies confirm the present study results.

In the present study, the highest frequency of meningitis was reported after fall. In Hatami et al., study in Kermanshah Province; most cases of meningitis were also reported in fall, which agree with the

present study [14]. Contrary to these results, Kanani et al., reported the highest frequency of meningitis in Kurdistan during spring [7]. Furthermore, since in the present study, viral meningitis rate was greater than other types and most aseptic meningitis are caused as a result of viruses, especially Enteroviruses, with prevalence in early fall [1]; the difference can thus be explained.

In this study, the rate of viral meningitis was greater than bacterial meningitis, which is in Ghasemi et al., study (56.2% viral against 37% bacterial) [13]. Unlike the present study, in studies conducted in Kurdistan and Khuzestan, bacterial meningitis rate was greater than viral meningitis (66.5% bacterial and 33.5% viral [7], and 68.9% bacterial and 27.1% viral [12] respectively [7,12]. To explain the difference, it should be asserted that in addition to geographical difference, because the diagnosis of meningitis was predominantly performed through CSF analysis in the present study, some bacterial meningitis cases might have been diagnosed as viral.

Among patients whose meningitis had been caused by bacterial factors (10.3%), most bacterial types were *Streptococcus pneumonaiee* and *Meningococcal*. Like the present study, in another study in Tehran, found *Streptococcus peneumoniaeas* the most common microorganism [13]. In a study conducted in Italy, the most common known cause of bacterial meningitis was pneumococcal (24.6%) and meningococcal (18%) [5]. In another study, *Streptococcus pneumonaiee* and *Neisseria meningiditis* were the most common causes of bacterial meningitis [16]. The difference in bacterial factors in various studies can be attributed to a variety of local bacteria, geographical conditions, and vaccination programs [12].

In the present study, of the patients' records that were complete in terms of risk factors, the highest risk factors were head trauma, upper respiratory infection, and drug addiction, respectively. In a study conducted in Kurdistan-Iran, head trauma, neurosurgery, and craniotomy were predisposing factors for meningitis [7]. In Germany, Kastenbauere and Pfister regarded ear and sinus infections, dural fistula, diabetes and *pneumonaie* the most common causes of meningitis [9]. In another study in France, dural fistula and sinusitis were proposed as meningitis risk factors [4]. Although in most of the above studies, similar risk factors have been proposed, risk factors and their percentages in the present study may differ due to incomplete data and small sample size.

In the present study, the triad of classic signs of meningitis including fever, headache, and stiff neck were observed in 16.7% of patients. In Alavi et al., study, this rate was 12% [12]. In another study conducted on patients with bacterial meningitis, 44% of patients experienced these signs [10]. Mean while, in a study by Kanani et al., meningitis triad was reported in 80% of cases. In the present study, clinical signs had not been fully recorded in 50.4% of cases, which can explain these differences. Thus, based on the present study results, the importance of recording and controlling patients' data in hospitals, for further actions, should be emphasized.

In the present study, CSF culture results of patients with meningitis were positive in only 10.3% of cases, and negative in 46.7% of patients. No CSF culture results had been reported for other patients. In a study by Alavi et al., positive CSF culture results were 19.5% [12] while in another study, 23.4% of CSF cultures were positive [7]. Studies conducted in other countries report higher statistics. In a study, CSF culture was positive in 75.9% of patients [9]. In a study by Kim et al., positive CSF culture was reported in 34% of cases [17]. There are different reasons for false negative CSF culture results including use of antibiotics prior to culture, inappropriate LP sampling method, neglecting technical points when handling samples, incorrect culture, and use of other diagnostic techniques [12]. In the present study, 57.4% of patients received antibiotics before LP. Also, it is possible that a number of patients may have been under several antimicrobial treatments, which could have affected test results. In such cases, other diagnostic methods such as PCR are recommended [1], which had not been performed for patients in any of Mazandaran hospitals.

In the present study, median of cerebrospinal fluid sugar in patients with bacterial meningitis was 50 mg/dl, which disagrees with results of other studies [5], since, despite diagnosis of bacterial meningitis, median cerebrospinal fluid sugar in patients was higher than 40 mg/dl. As use of antibiotics before hospitalization or performing LP could kills bacteria, use of sugar is reduced [18]. Furthermore, some patients may have had their blood sugar increased because of stress due to hospitalization. Since CSF sugar is about 2/3 of concurrent blood sugar, and this ratio increases with increasing blood sugar [2,19], high level of CSF sugar in patients with bacterial meningitis may be justified.

In the present study, leukocyte values in bacterial meningitis were higher than 1000, which concurs with the results of other studies [5]. However, this value was also higher than 1000 in viral meningitis, which disagrees with Alavi et al., results [12]. Cell count less than 100 is usually more common in patients with viral meningitis. But, since peripheral blood in CSF sample, following LP can increase white blood cells in cerebrospinal fluid [19], lumber puncture technique could have caused this abnormal rise. Studies show polymorphonuclear dominance in bacterial meningitis, while in viral type, lymphocytes are dominant [19], and the present study results also confirm this.

In this study, of the total patients with known results (117 patients, 86.9%), hospital mortality rate was reported 8.8%, which concurs with results of Ghasemi et al., [13]. In another study in Iran, this rate was reported 5.39% and in other countries, patient mortality rate was 24.1% [9] and 25% [4]. However, these studies were conducted only on patients with bacterial meningitis, and as nearly 30% of adults with bacterial meningitis die of this disease [1]; the difference in results are justified.

Successful treatment results of patients depend upon proper and prompt use of antibiotics. Use of Betalactams and Vancomycin in patients' drug regimen is cited in various studies [20]. In the present study, the most frequent drug regimen included ceftriaxone and Vancomycin in 22.9% of patients. In Kim et al., study, combined ceftriaxone and Vancomycin was used in 22.9% of patients, and Ceftazidime and Vancomycin in 68.7% [17].

STUDY LIMITATIONS

Since this was a retrospective study, limitations included incomplete patient records. Moreover, a number of records of patients whose meningitis report existed in the Provincial Health Center could not be found in hospital. Hence, further more studies are required, given the incomplete record system in hospitals, and it is recommended that a longitudinal study be conducted in future.

CONCLUSION

Over the last 7 years, viral meningitis has had the highest frequency in Amol city. The biggest risk factors include head trauma, upper respiratory infection, and drug addiction, respectively. The most common clinical symptoms include headache with fever, nausea and vomiting, and stiff neck, and the most important diagnostic procedure include analysis, smear, and culture of cerebrospinal fluid. It can be recommended to perform a longitudinal study during the coming years on patients with meningitis.

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Author	Year	Country	Sample size	Gender		Type of meningitis		Clinical sign		Type of organism		Mortality rate
Present study	2006 to 2012	Iran	137	Male	71.5%	viral	53.9%	Headache	40.1%	*Streptococcus pneumonaie*	5.2%	8.8%
						bacterial	46%	Fever	37.2%	Meningococcus	3.7%	
				Female	28.5%	fungal	0.7%	Nausea and vomiting	32.8%	Staphylococcus	0.7%	
						unknown	1.4%	stiff neck	19.7%	Neisseria-meningitidis.	0.7%	
								Loss of consciousness	15.3%			
Alavi et al., [12]	2003 to 2007	Iran	312	Male	60.5%	Bacterial	68.9%	Fever	96.7%	Meningococci	47.6%	5.39%
				Female	39.5%	Aseptic	31.1%	Stiff neck	91.6%	Pneumococci	38.1%	
								Loss of consciousness	13.1%	Haemophilus influenza	9.6%	
										Klebsiella	4.7%	
Abdi Liaei et al., [8]	1991 to 2001	Iran	131	Male	75%	Acute Bacterial Meningitis		Loss of consciousness	64.9%	Pneumococci	30.5%	21%
				Female	25%					Meningococci	18.3%	
Nur et al., [21]	2001 to 2005	Malaysia	47	Male	62%	Bacterial Meningitis		Fever	83%	*Streptococcus pneumonaie*	23%	15%
				Female	38%			vomiting	25.5%			
								Headache	23%	*Haemophilusin fluenzae*	15%	
								Seizures	23%			
								Loss of consciousness	11%	*Escherichia coli*	8.5%	
Chang et al., [22]	1999 to 2005	Taiwan	181	Male	72%	Bacterial Meningitis		Fever	88%	*Klebsiella pneumonaie*	25.5%	30.3%
				Female	28%			Alter consciousness	59.6%			
								Seizures	36%	*Acinetobater*	11.5%	
Tsai et al., [23]	1986 to 2003	Taiwan	62	Male	77%	Bacterial Meningitis		Impaired consciousness–thrombocytopenia -		*Klebsiella pneumonaiee*	19%	20%
				Female	23%					*Pseudomonas aeruginosa*	14.5%	
Mai et al., [24]	1996 to 2005	Vietnam	450	Male	77.5%	Bacterial Meningitis		Headache	94.0%	*Streptococcus suis*	33.6%	2.6%
				Female	22.5%			Stiff neck	94.0%	*Streptococcus pneumonaie*	18%	
								Vomiting	66.2%	*Neisseria meningitides*	6.5%	
Ayaz et al., [25]	1998 to 2002	Turkey	186	Male	60 %	Bacterial Meningitis		Headache	92.5%	Gram-positive cocci	26%	15.6%
				Female	40 %			Fever	88.2%	*Streptococcus pneumonaie*	12%	
								Stiff neck	80.1%	Gram-negative cocci	10%	
Khan et al., [26]	2001 to 2009	India	403			Bacterial Meningitis		Fever	96%	*Staphylococcus aureus*	37.7%	17.4%
										Streptococcus species	8.7%	
								Headache	33%	*Enterococcus faecalis*	4.5%	
								Stiff neck	51%	*Streptococcus pneumonaiee*	8.2%	
								Unconsciousness	62%	Enterobacteriaceae family	20.3%	

[Table/Fig-3]: Findings of some studies in Iran and similar demographic region

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