Med. J. Cairo Univ., Vol. 90, No. 1, March: 185-193, 2022
www.medicaljournalofcairouniversity.net

Value of Cerebrospinal Fluid Calprotectin Assay in Patients with Acute Meningitis

MOHAMMAD E. EL SHEWI, M.D.* and SHOZAN A. ALI, M.D.**

The Departments of Hepatology, Gastroenterology & Infectious Diseases and Medical Biochemistry**, Faculty of Medicine, Benha University*

Abstract

Background: Meningitis is an inflammation of the protective membranes covering the brain and spinal cord. Acute meningitis could be life-threatening condition because of the inflammation's proximity to the brain and spinal cord. Therefore, immediate diagnostic and therapeutic procedures were required.

Aim of Study: This study aimed to assess the diagnostic usefulness of measuring cerebrospinal fluid (CSF) calprotectin level indiagnosis of acute meningitis and its value in differentiation between bacterial and nonbacterial (aseptic) acute meningitis.

Patients and Methods: This study conducted on 90 subjects, sixty patients represented to Shebin El-Koum Fever Hospital with acutely suggesting symptoms of meningitis (fever, severe headache, altered mental status, avoid bright light and stiff or painful neck) in whom lumber puncture was done and CSF conventional laboratory finding like WBCs count, glucose and protein were measured, these patients were divided into, group 1: Thirty patients with CSF laboratory finding of bacterial meningitis, group 2: Thirty patients with CSF laboratory finding of aseptic meningitis and group 3: Thirty cross age and sex matched non-meningitc subjects undergoing spinal anesthesia for non-neurological surgical causes as acontrol group. The concentration of CSF calprotectin was determined by ELISA in all the studied cases.

Results: CSF calprotectin mean level was 10.2±SD 2.36 ng/ml in patients with bacterial meningitis, 8.7±SD 1.91 ng/ml inaseptic meningitis while, in the control group was 6.5±SD 1.45ng/ml with statistically significant difference ($p<0.01$) between all groups. Performance of CSF calprotectin in diagnosis of aseptic meningitis at a value 7.42-9.03ng/ml by ROC curve parameter had sensitivity 60%, specificity 60%, PPV 60%, NPV 60%, AUC: 0.68 with 95% CI, 0.55-0.82. While at a value more than 9.03ng/ml, CSF calprotectin hadsensitivity 80%), specificity (70%), PPV 72.7%, NPV 77.8%, AUC: 0.81 with 95% CI, 0.72-0.90 in diagnosis of bacterial meningitis.

Conclusions: CSF calprotectin may serve as a potential diagnostic marker of acute meningitis and its determination could be usefulin differentiation between bacterial and aseptic meningitis.

Key Words: *Calprotectin – Cerebrospinal fluid – Acute meningitis – Bacterial – Aseptic.*

Correspondence to: Dr. Mohammad E. El Shewi, The Department of Hepatology, Gastroenterology & Infectious Diseases, Faculty of Medicine, Benha University

Introduction

MENINGITIS is an inflammatory disease of the leptomeninges, the tissues surrounding the brain and spinal cord, and is defined by an abnormal number of white blood cells in the CSF [1]. Bacterial meningitis is a medical emergency, and immediate steps must be taken to establish the specific cause and initiate effective therapy [2]. The possible presence of bacterial meningitis is suggested by the symptoms of fever, altered mental status, headache and nuchal rigidity. Virtually all patients have at least one of the classic triads of fever, neck stiffness and altered mental status [3]. Despite the effectiveness of current antibiotics in clearing bacteria from the cerebrospinal fluid, bacterial meningitis continues to cause significant morbidity and mortality [4]. Streptococcus pneumoniae is the mostcommon bacterial etiology of meningitis in adults of all ages. The frequency of other pathogens as Neisseria meningitides and Haemophilus influenza has varied incidence in different situations [5]. Aseptic meningitis refers to patients who have clinical and laboratory evidence for meningeal inflammation with negative routine bacterial cultures. The most common cause is enterovirus. Additional etiologies include (mycobacteria, fungi, spirochetes), parameningeal infections, medications, and malignancy [6]. Every year more than 1.7 million people worldwide suffer meningitis. Even with prompt diagnosis and treatment, approximately 10% of patients die and up to 20% or more sustain disability [7]. Calprotectin is produced by

activated monocytes and microglia, and CSF level could be a marker of neuroinflammation, which was detectable in CSF from 13.8% of normal controls, compared to 90.5% of patients with neurological infections [8]. In this study we supposed calprotectin as an inflammatory marker could differentiate between bacterial and aseptic meningitis.

Material and Methods

This prospective study was conducted on 90 subjects, sixty of them were clinically suspected to have acute meningitis (high fever, severe headache, altered mental status, avoid bright light and stiff or painful neck)and were admitted to Shebin El-Koum Fever Hospital and 30 non-meningitc subjects undergoing spinal anesthesia for non-neurological operations were recruited from Surgical Department of Benha University Hospitals during 2018 as a control group. Patients with history or on therapy of autoimmune disease, head trauma and immunocompromised were excluded. Also, patients with CT evidence of space occupying lesion in brain CT (abscess, tumor ... etc.) were excluded.

The studied subjects were subdivided into the following groups:

Group I: Acute bacterial meningitis according to CSF laboratory finding,WBC count is elevatedusually in the range of 1000-5000 cells/mm^3, although this range can be quite broad (>100 cells/mm^3) with at least 80% neutrophils predominance, an elevated protein (>100mg/dl) and decreased glucose (<40mg/dl) [9].

Group II: Acute aseptic meningitis in whomWBCs of <50 cell/mm^3 of and >50% were mononuclear/lymphocyte cells with the absence of any septic meningitis laboratory criteria [an elevated protein (>100mg/dl) or decreased glucose (<40mg/dl)] [9].

Group III: Thirty CSF of non-meningitc subjects undergoing spinal anesthesia for non-neurological surgical operations recruited from surgical departments of Benha University Hospitals as a control group.

All patients will be subjected to the following:

1- Full medical history: Including personal history including (name, age, sex and locality) - history of present illness including (fever, headache, altered mental status, vomiting) and antibiotic drug intake before admission and duration of it.

2- Complete clinical examination for all systems including nervous system with special stress on signs of meningitis (neck rigidity-kerning's sign-Brudhzinski sign), skin rash and focal neurological signs.

3- Investigations:

- Routine laboratory study in the form of: Complete blood count, serum creatinine and urea, ESR and CRP and liver enzymes (ALT, AST).
- Brain CT without contrast is necessary incases with focal neurologic deficits, papilledema, recent seizures and abnormal level of consciousness [10] and to exclude other causes e.g., abscess, tumor ... others.
- Lumbar puncture and CSF analysis.

Maneuver of lumbar puncture:

The patient should assume either the lateral recumbent position or a sitting position. The lateral recumbent position is preferred, to obtain an accurate opening pressure and to reduce the risk of post-puncture headache.Insert the needle in the intervertebral space between L3 and L4 or L4 and L5, because these points are below the termination of the spinal cord. The CSF was withdrawn by lumbar puncture under aseptic precautions into a sterile glass test tube and immediately transported to the laboratory [11]. The studied patients had undergone a complete biochemical and physical-examination of the CSF for diagnosis of acute meningitis.

CSF is examined for the following:

a- Physical examination: e.g., color and aspect.

b- Chemical examination: Protein, glucose and manual microscopic cell counting: Using Fuchs-Rosenthal counting chambers (hemocytometer) for both RBCs and WBCs.

c- Bacteriological examination: CSF culture on:

1- Blood agar and chocolate agar plates incubated at 37°C for 72 hours in 5-10% CO_2 for evidence of growth N. meningitides, St. pneumonae and H. influenzae type B.

2- MacConkey's agar, incubated at 37°C for 72 hours for evidence of growth of Escherichia coli, Salmonella enteritidis, Klebsiella pneumonia and Proteus mirabilis [11].

d- An aliquot of the CSF (2mL) was stored in a freezer at a temperature of –20ºC for later determination of calprotectin. The determination of calprotectin levels in CSF employs an in-vitro double-antibody sandwich enzyme-linked immune-sorbent assay (ELISA) to measure the

level of Calprotectin in CSF samples by using commercially kit Shanghai Sunred Biological Technology, China (with the assay range 0.15ng/ml -> 40ng/ml and sensitivity 0.142ng/ml). Antibody specific for calprotectin has been pre-coated onto a microplate. Standards and samples were pitted into the wells and any calprotectin present is bound by immobilized antibody. Following a wash to remove any unbound avidin-enzyme reagent, a substrate solution is added to the wells and color develops in proportion to the amount of calprotectin bound in the initial step. By TECAN Infinite F50 ELISA with Magellan Tracker software (Tecan Trading AG, Switzerland), standard dilution of calprotectin was measured.

Statistics: The collected data were tabulated and analyzed using SPSS version 16 software (SPSS Inc, Chicago, ILL Company). We used the parameters derived from the ROC curves for the assessment of diagnostic accuracy: The AUC, sensitivity, specificity, positive like hood ratio, negative likehood ratio and the cut-off (cut point) value of the respective parameters corresponding with the highest Youden index. Graphical correlation of calprotectin ROC curve was done.

Results

Table (1): Socio-demographic characters of the studied patients.

Variable	No. (N=90)	% (100%)
The studied groups:		
Bacterial meningitis	30	33.3
Aseptic meningitis	30	33.3
Controls	30	33.3
Age (ys):		
Mean ±SD	34.0±12.9	
Range	18-60	
Sex:		
Male	55	61.1
Female	35	38.9
Occupation:		
Employee	48	53.3
Not working	42	46.7
Marital status:		
Single	50	55.6
Married	39	43.3
Widow	1	1.1
Smoking:		
No	65	72.2
Yes	25	27.8

Table (2): Comparing the studied groups of patients regarding clinical examination.

Variable	Bacterial meningitis (N=30)		Aseptic meningitis (N=30)		X^2	*p*
	No.	%	No.	%		
Fever:						
Yes (N=53)	28	93.3	25	83.3	0.54	0.48
No (N=7)	2	6.7	5	16.7		(NS)
Headache:						
Yes (N=44)	23	76.7	21	70	0.47	0.62
No (N=16)	7	23.3	9	30		(NS)
Brudzniski sign:						
Yes (N=30)	20	66.7	10	33.3	6.67	0.01
No (N=30)	12	40	18	60		(S)
Rash:						
Yes (N=7)	4	13.3	3	10.0	FET	1.0
No (N=53)	26	86.7	27	90.0		(NS)
Convulsion:						
Yes (N=16)	9	30.0	7	23.3	0.34	0.56
No (N=44)	21	70.0	23	76.7		(NS)
Neck rigidity:						
Yes (N=33)	23	76.7	10	33.3	11.4	0.001
No (N=27)	7	23.3	20	66.7		(HS)
Kering's sign:						
Yes (N=30)	19	63.3	11	36.7	4.27	0.039
No (N=30)	10	33.3	20	66.7		(S)

Table (3): Comparing the studied groups regarding serum CRP.

	Groups		Controls	Total
	Bacterial meningitis	Aseptic meningitis		
CRPs (mg/dl):				
+ve >6:				
Count	24	5	1	30
%Within Group	80.0%	16.7%	3.3%	33.3%
–ve <6:				
Count	6	25	29	60
%Within Group	20.0%	83.3%	96.7%	66.7%
Total:				
Count	30	30	30	90
%Within Group	100.0%	100.0%	100.0%	100.0%

X^2=45.3 *p*<0.001 (HS).

Table (4): Comparing the studied groups regarding CSF aspect.

	Groups		Controls	Total
	Bacterial meningitis	Aseptic meningitis		
Aspect:				
Clear:				
Count	3	24	30	57
% Within Group	10.0%	80.0%	100.0%	63.3%
Hazy:				
Count	27	6	0	33
% Within Group	90.0%	20.0%	.0%	36.7%
Total:				
Count	30	30	30	90
% Within Group	100.0%	100.0%	100.0%	100.0%

Table (5): WBCs and PMN% in the peripheral blood finding in the studied patients.

Group	N	WBCs (x 10^3)			ANOVA	*p*	Sig pairs
		Mean	± SD	Range			
Bacterial meningitis	30	15.15	6.48	6.9-44	30.02	<0.001 (HS)	Bacterial controls
Aseptic meningitis	30	10.23	3.53	519			Aseptic controls
Controls	30	6.30	2.01	4-11			Bacterial aseptic
		PMN%					
Bacterial meningitis	30	90.3	12.15	54.8-99	67.2	<0.001 (HS)	Bacterialcontrols
Aseptic meningitis	30	68.1	10.05	53.8-91			Aseptic controls
Controls	30	59.6	9.29	45-80			Bacterialaseptic
		ESR (mm/hr.)					
Bacterial meningitis	30	41	32.09	23-110	18.7	<0.001 (HS)	Bacterialcontrols
Aseptic meningitis	30	38	26.87	22-90			Aseptic controls
Controls	30	6	7.36	3-34			Bacterialaseptic

Table (6): CSF laboratory finding in the studied groups.

Group	N	Leucocytes (N=0-5 cells/hpf)			ANOVA	*p*	Sig pairs
		Mean	± SD	Range			
Bacterial meningitis	30	878.5	1430.9	11-8000	75.2*	<0.001 (HS)	Bacterial controls
Aseptic meningitis	30	108.6	164.0	10-770			Aseptic controls
Controls	30	0.03	0.18	0-1			Bacterial aseptic
		PMN%					
Bacterial meningitis	30	79.1	12.93	55-100	259.8	<0.001 (HS)	Bacterialcontrols
Aseptic meningitis	30	9.8	10.54	0-40			Aseptic controls
Controls	30	3.3	18.25	0-100			Bacterialaseptic
		Protein (n=15-45 mg/dl)					
Bacterial meningitis	30	148.2	72.3	70-365	46.4	<0.001 (HS)	Bacterialcontrols
Aseptic meningitis	30	71.0	23.6	18-129			Aseptic controls
Controls	30	39.2	17.41	15-91			Bacterialaseptic
		Glucose (45-70 mg/dl)					
Bacterial meningitis	30	41.8	12.1	8-58	15.9	<0.001 (HS)	Bacterialcontrols
Aseptic meningitis	30	64.1	18.7	35-152			Aseptic controls
Controls	30	53.9	14.3	28-78			Bacterialaseptic

Table (7): CSF culture results among the studied meningitc patients.

	Groups: Total (60)		
	Bacterial meningitis	Aseptic meningitis	
CSF culture:			
–ve:			
Count	7	30	37
%Within Group	23.3%	100.0%	61.7%
Meningococci:			
Count	7	0	7
%Within Group	23.3%	.0%	11,7%
Pneumococci:			
Count	11	0	11
%Within Group	36.7%	.0%	18,3%
Hemophilus:			
Count	3	0	3
%Within Group	10.0%	.0%	5%
Staphylococci:			
Count	1	0	1
%Within Group	3.3 %	.0%	1.7%
E. coli:			
Count	1	0	1
%Within Group	3.3 %	.0%	1.7%
Total:			
Count	30	30	60
%Within Group	100.0%	100.0%	100.0%

Table (8): CSF Calprotectin in the studied groups.

Group	N.	Calprotectin (ng/ml)				St."t"	*p*	Sig pairs
		Mean	± SD	Median	Range			
Bacterial meningitis	30	10.2	2.36	9.71	5.64-14.96	2.64	0.011 (S)	Bacterial controls
Aseptic meningitis	30	8.7	1.91	8.68	5.56-13.3			Aseptic controls
Controls	30	6.5	1.45	6.38	4.05-9.76			

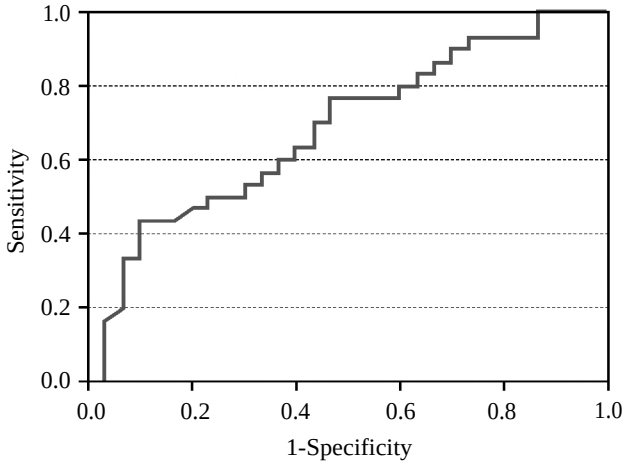

Fig. (1): Performance of calprotectin in diagnosis of aseptic meningitis.

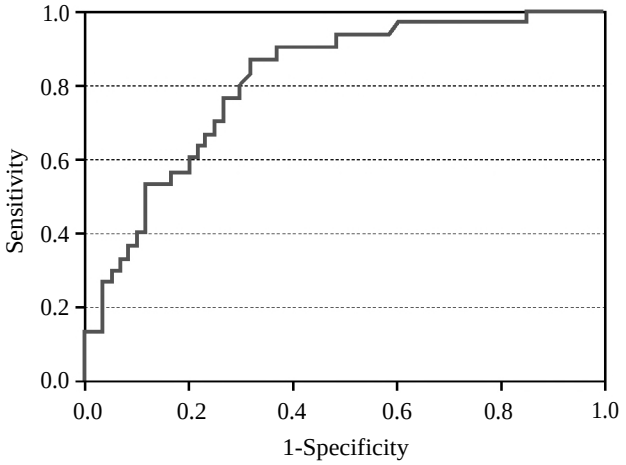

Fig. (2): Performance of calprotectin in diagnosis of bacterial meningitis.

Calprotectin	Sens %	Spec %	PPV %	NPV %	AUC	95% CI	*p*
7.42-9.03	60%	60%	60%	60%	0.68	0.55-0.82	0.014

Cal-protectin	Sens %	Spec %	PPV %	NPV %	AUC	95% CI	*p*
>9.03	80%	70%	72.7%	77.8%	0.81	0.72-0.90	<0.001 (HS)

Discussion

Meningitis is the main infectious disease ofthe central nervous system (CNS) [12]. It is an inflammation of the protective membranes covering the brain and spinal cord, known collectively as the meninges [13]. Calprotectin was originally discovered as an antimicrobial protein that was present in the cytoplasm of neutrophilic granulocytes [14]. Subsequently, it has been recognized as a promising marker of inflammation or rather a trace of the antagonism going on inside the organism [15]. Furthermore, the molecule is involved in the recruitment ofinflammatory cells by interactions with endothelial cells [16]. Bacterial meningitis is a medical emergency, and immediate steps must be taken to establish the specific cause and initiate effective therapy [2]. Therefore, immediate diagnostic procedures were required to differentiate between septic and aseptic meningitis. This studyaimed to assess the diagnostic usefulness of measuring cerebrospinal fluid calprotectin level for differentiation between bacterial and aseptic meningitis. In this study it was found that, no age was immune against meningitis in both septic (32.6± 13.62) and aseptic groups (33.5±12.32). These results were in agreement with those of [17] who-found that, high frequency of infection occurred in adult group which represented about 71% of all cases. In the present study, the infection in septic group in males (66.7%) was higher than females (33.3%). In addition, the rate of infection in aseptic group in males (60%) was higher than female (40%). The rate of infection in males (55.7%) was higher than females (44.2%) with male to female ratio 1.3:1; with disagreement of the previous studyby [18] who found that male ratio was 86.56% vs. eighteen (13.43%) was femalemostly due to selection bias. In the present study, fever was the most frequent symptom; fever was present in 93.3% of bacterial meningitis groupand 83.3% in aseptic meningitis group. This result is nearly the same as Ibrahim and his colleagues, who found that, among the patients with acute bacterialmeningitis, 95% had fever and Choi and his colleagues, who found that, among the patients of aseptic meningitis, 92.9% had fever [19,20]. In this study, headache was present in 76.7% in bacterial meningitis group

and 70% in aseptic meningitis group. This finding is approximately similar to those of [17] who found that, among the patients with acute bacterial meningitis 56.1% had headache and to [19] who found that, among the cases of aseptic meningitis 57.1% had headache. Convulsionsin this study had no significant difference between bacterial meningitis group (30%) and aseptic group (23.3%) as in Table (2). Dubos and his colleagues, found that, there was no significant difference in occurring of convulsions between patients with acute bacterialnd aseptic meningitis [21]. This study showed that, signs of meningeal irritation as neck rigidity is present in 76.7% in bacterial meningitis group and 33.3% of cases of aseptic meningitis group patients as in Table (2). Kernig sign detected byplacing the patient supine with hip flexed at 90 degrees. Attempt to extend the leg at the knee. The test is positive when there is resistance to extension at the knee to > 135 degrees or pain in the lower back or posterior thigh. Kernig sign is present in 63.3% in bacterial meningitis group and in 36.7% in aseptic meningitis group as in Table (2). Brudzinski sign detected by placing the patient in the supine position and passively flex the head toward the chest. The test is positive when there is flexion of the knees and hips of the patient. Brudzinski sign is present in 66.7% in bacterial meningitis group and in 33.3% in aseptic meningitis group as in Table (2). This result was partially similar to those reported by Ndreu and his colleagues, who found that, neck rigidity, meningeal signs were present in 77.1% and 75% of cases of septic meningitis respectively [22]. But this result partially agrees with Michael and his colleagues, who found that, neck rigidity in cases of aseptic meningitis was (66%) while, in the cases of bacterial meningitis was (29%) [23]. This study showed that, there were highly significant difference between bacterial meningitis group and aseptic meningitis groupregarding peripheral leucocytic count which was (15150±6.48) in bacterial meningitis group and (10230±3.53) in aseptic meningitis group (p<0.001). These results were in agreement with Makoo et al. and Alkholi et al., who found that, there was a statistically significant difference between patients with bacterial meningitis and those with viral meningitis regarding the mean peripheral blood WBCs [24,25]. In contrast to Singhi and his colleagues,who stated that, there is no significant difference in peripheral blood WBCs between the patients with bacterial and aseptic meningitis (p=0.36). This study showed that polymorphs percentage in peripheral blood WBCs were higher in septic group (90.3±12.5) than aseptic group (86.1±10.05) with (p<0.001). These results were in agreement with [20,25] who stated that there is statistically significant difference in values of polymorphs at admission between patients with bacterial meningitis and those with aseptic meningitis with higher values in septic meningitis. The increased TLC in bacterial meningitis may be attributed to increased release of leukocytes from bone marrow storage pools in response to bacterial infection [26]. The present study revealed highly significant increase in erythrocyte sedimentation rate (ESR) in bacterial meningitis group (41.2± 32.09) when compared to aseptic meningitis group (38.4±26.87) (p<0.001) and also significant increase in C-reactive protein in patients with bacterial meningitis than patients with aseptic meningitis and those with control group. It was positive in 80% of bacterial meningitis group of patients but it was positive in 16.7% of aseptic meningitis group of patients and positive in 3.3% in the control group. These results were in agreement with [27] who stated that, there were statistically significant differences in ESR (p<0.007) and CRP (p<0.001) between patients with bacterial meningitis and those with aseptic meningitis. This disagreement maybe explained by the fact that, the peripheral white blood cells and ESR can be different very early in the disease and in patients partially treated by antibiotics. Peripheral white blood cells and ESR are acute phase reaction which are usually elevated in bacterial meningitis but are of limited diagnostic value especially in atypical cases. Additionally, the above-mentioned acute phase reactants can bedifferent very early in the disease and in patients partially treated by antibiotics [28]. The present study described a statistically significant difference in aspect of CSF between bacterial meningitis group compared to theaseptic meningitis group. It was hazy in 90% of patients of bacterial group but, it was hazy in 20% of aseptic meningitis groupas in Table (4). This result is similar to El-Kapany, who stated that there was statistically significant difference in aspect of CSF between patients of bacterial and aseptic meningitis [29]. In the present study, statistical analysis revealed highly significant increase in CSF protein (p<0.001) in bacterial meningitis group of patients (148.2± 72.3mg/dl) than in aseptic meningitis group of patients (71±23.6mg/dl). Also, there is significant increase in CSF-WBCs count (p<0.001) in bacterial group (878.5±1430.9) than in the aseptic group (108.6±164). Highly significant decrease in CSF-glucose (p<0.001) in bacterial meningitis group-patients (41.8± 12.1) when compared to aseptic meningitis (64.1±18.7), as well as in aseptic meningitis group patients when compared to control group (53.9±14.3). Moreover, CSF-PMN (p<0.001)

cells were predominant in bacterial meningitis group patients (79.1±12.93) than in aseptic meningitis group patients with (9.8±10.54) as in Table (5). These findings agree with Makoo et al. and Alkholi et al., who stated that, there were high statistically significant differences (p<0.001) between bacterial and aseptic meningitis patients regarding CSF leukocyte count, CSF protein and CSF glucose [24,25]. In this study, CSF culture was positive in 23 patients with bacterial meningitis group (76.7%) while, it was negative in 7 patients of the same group (23.3%). Statistical analysis of CSF culture results revealed that, the detected bacteria were pneumococci (gram positive cocci) in 11 patients (36.7%), meningococci (gram negative diplococci) in 7 patients (23.3%), H.influenzae (gram negative pleomorphic rods) in 3 patient (10%), Staph.aureus in 1 patient (3.3%) and E.coli (gram negative bacilli in 1 patient (3.3%) as in Table (7). These results agree Dubos and his colleagues, who stated that, CSF gram stain revealed bacteria in 75% of bacterial meningitis [21]. In contrast to Makoo and his colleagues who detected organisms in only 16% of their patients, this difference may be due to few numbers of organisms in CSF, incorrect culture techniques, delay in sending the samples to thelaboratory and antibiotic administration before sampling [24]. These results were nearly the same of Alam and his colleagues in Egypt, who found that, S. pneumoniae was the most common organism isolated (47.4%) followed by N. meningitides (33.9%), H. influenza (10.2%) and other gram-negative bacteria (8.5%) [30]. The results of this study revealed high level of CSF calprotectin in bacterial group (10.2±2.36ng/ml) when compared with aseptic meningitis (8.7± 1.91ng/ml) and (p>0.011) as in Table (8). Calprotectin levels in CSF raised in patients with multiple sclerosis (23.7ng/ml) when compared with normal control (13.8ng/ml) with the reference range was 5ng/ml [8]. In this study, using a cut-off calprotectin level >7.42ng/mL clearly distinguished patients with meningitis group (all patients with bacterial and aseptic meningitis had CSF calprotectin level above this level) from control with sensitivity 60%, specificity 60%, AUC 0.88 and (p>0.011), while using a cutoff calprotectin level >9.03ng/ml differentiate patients with bacterial-meningitis from those with aseptic meningitis with sensitivity 80%, specificity 70% and (p>0.011). These results go in line with a study carried on 73 patients 23 patients of them had bacterial meningitis and 50 of them had aseptic meningitis which revealed that calprotectin had the ability to differentiate between bacterial and aseptic meningitis however lactoferrin, polynuclear count and lactate concentration in CSF showed a very good diagnostic efficiency as well [31]. Also, Berg Hansen stated that calprotectin was detectable in 13.8% of normal control, compared with 90.5% of patients with neurological infection [8]. Because of calprotectin, as an acute phase reactant, plays vital physiological roles in infection and inflammation. It serves as a potential diagnostic marker for various inflammatory diseases [32]. So, the determination of calprotectin in the CSF could differentiate between bacterial and aseptic meningitis. However, Calprotectin was far less efficient diagnostic marker and further studies are warranted to define the useful CSF cut-off for the diagnosis of bacterial and aseptic meningitis. The drawback of this study was the definitediagnosis of viral cause of acute aseptic meningitis by serum or CSF PCR had not been done due to limited availability and technical obstacles. Also, number of noninfectious causes and other infectious etiologies as well, were not determined.

Acknowledgment:

The authors would thank the staff of the Shebin El-Koum fever hospital, Dr. Mohamoud Salam and Benha Faculty of Medicine Medical Biochemistry Department, and the laboratory technicians, for their valuable efforts.

Funding: None.

Conflicts of interest: None.

Ethical approval: Approved.

References

1- MANDELL G.L., BENNETT J.E. and DOLIN R.: Approach to the Patient with Central Nervous System Infection. In: Principles and Practice of Infectious Diseases, 7th ed., Philadelphia, Vol. 1, p. 1183, 2010.

2- COTTAGNOUD P. and TÄUBER, M.G.: Fluoroquinolones in the Treatment of Meningitis. Curr. Infect Dis. Rep., 5: 329, 2003.

3- VAN DE BEEK D., DE GANS J., SPANJAARD L., WEISFELT M. et al.: Clinical features and prognostic factors in adults with bacterial meningitis. N. Engl. J. Med., 351: 1849-1859, 2004.

4- CASTELBLANCO R.L., LEE M. and HASBUN R.: Epidemiology of bacterial meningitis in the USA from 1997 to 2010: A population-based observational study. Lancet Infect Dis., 14: 813, 2014.

5- TSAI C., GRIFFIN M.R., NUORTI J. and GRIJALVA C.G.: Changing epidemiology of pneumococcal meningitis after the introduction of pneumococcal conjugate vaccine in the United States. Clin. Infect Dis., 46: 1664, 2008).

6- KUDESIA G. and MCKENDRICK M.W.: Clinical features of viral meningitis in adults: Significant differences in cerebrospinal fluid findings among herpes simplex virus, varicella zoster virus, and enterovirus infections. Clin. Infect Dis., 47: 783, 2008.

7- World Health Organization: Meningococcal Meningitis Factsheet N°141. Viewed 4 March 2013, s6,7, 2012.

8- BERG-HANSEN P., VANDVIK B., FAGERHOL M. and HOLMOY T.: Calprotectin levels in the cerebrospinal fluid reflect disease activity in multiple sclerosis. Journal of Neuroimmunology, Volume 216: 98-102, 2009.

9- World Health Organization: Vaccine research and development. In: Generic protocol for population-based surveillance of Haemophilus influenzae type B. Geneva: World Health Organization, 1996.

10- ELLENBY M.S., TEGTMEYER K., LAI S. and BRANDER D.A.: Lumbar puncture. N. Engl. J. Med., 355: 12, 2006.

11- COLLEE J.G., DUGUID J.P., FRASER A.G., MAMION B.P. et al.: Laboratory strategy in the diagnosis of infective syndromes. Churchill Livingstone, 1 (4): 53-94, 1996.

12- DE ALMEIDA S.M., NOGUEIRA M.B., RABONI S.M. and VIDAL L.R.: Laboratory diagnosis of lymphocytic meningitis. The Brazilian Journal of Infectious Diseases, 11 (5): 489-49, 2007.

13- SAEZ-LLORENSM X. and MCCRACKEN G.H.: Central nervous system infections. In: Long SS, Pickering L.K., Prober C.G. Principals and practice of pediatric infectious diseases. 2nd ed. New York: Elsevier Science, p. 264-271, 2003.

14- DALE I., FAGERHOL M. and NAESGAARD I.: Purification and partial characterization of highly immunogenic human leukocyte protein, the L1 antigen. Eur. J. Biochem., 134: 1-6, 1983.

15- SANDER J., FAGERHOL M., BAKKEN J.S. and DALE I.: Plasma levels of the leukocyte LI protein in febrile conditions: Relation to etiology, number of leukocytes in blood, blood sedimentation reaction and C-reactive protein. Scand J. of Clin. LabI. Nvest., 44: 357-62, 1984.

16- SRIKRISHNA G., PANNEERSELVAM K., WESTPHAL V., ABRAHAM V., et al.: Two proteins modulating transendothelial migration of leukocytes recognize novel carboxylateglycans on endothelial cells. J. Immunol., 166: 4678-4688, 2001.

17- ABDUL RAB A., ALGOBATY F., SALEM A.K. and MOHAMMED Y.A.: Acute bacterial meningitis in adults: A hospital-based study in Yemen. Jpn. J. Infect Dis., 63: 128-131, 2010.

18- ABRO A.H., ABDOU A.S., ALI H., USTADI A.M., et al.: Cerebrospinal fluid analysis-Acute bacterial versus viral meningitis. Pak. J. Med. Sci., 24 (5): 645-650, 2008.

19- CHOI C.S., CHOI Y.J., HAN J.W., et al.: Clinical manifestations of CNS infections caused by Enterovirus type 71. Korean J. Pediatric, 54 (1): 11-16, 2011.

20- IBRAHIM K.A., ABDEL WAHAB A.A. and IBRAHIM A.S.: Diagnostic value of serum procalcitonin levels in children with meningitis: Acomparison with blood leucocyte and C-reactive protein. J. Pak. Med. Assoc., 61 (4): 346-51, 2011.

21- DUBOS F., KORCZOWSKI B., AYGUN D.A., MARTINOL A., et al.: Serum procalcitonin level and other biological markers to distinguish between bacterial and aseptic meningitis in children: a European multicenter case cohort study. Arch. Pediatric. Adolescent. Med., 162: 1157-1163, 2008.

22- NDREU A.H., SHYTAJ K.M., PILACA A.S. and HARXHI A.K.: Dexamethasone efficacy on bacterial meningitis - A retrospective analysis of Albanian adult patients. J. Infect D Ctries, 3 (11): 849-855, 2009.

23- MICHAEL B., MENEZES B. and CUNNIFFE J.: Effect of delayed lumbar punctures on the diagnosis of acute bacterial meningitis in adults. Emerg. Med. J., 27: 433-438, 2010.

24- MAKOO Z.B., AHADI N., MASHRABI O., HASANI A. et al.: Cerebrospinal fluid (CSF) Ferritin for differentiation of aseptic and bacterial meningitis in adults. Am. J. Infect. Dis., 6 (4): 98-102, 2010.

25- ALKHOLI U.M., ABD AL-MONEM N. and SULTAN M.H.: Serum procalcitonin in viral and bacterial meningitis. J. Global Infect Dis., 3: 14-8, 2011.

26- MARTIN C., BURDON P.C., BRIDGER G., GUTIERREZ-RAMOS J.C., et al.: Chemokines acting via CXCR4 and CXCR2 determines the release of neutrophils from the bone marrow and their return following senescence. Immunity, 19: 583-593, 2003.

27- YETKIN F., KAYABAS U., ERSOY Y., TOPLU S.A., et al.: Cerebrospinal Fluid Viscosity: A Novel Diagnostic Measure for Acute Meningitis. Southern Medical Journal, 103 (9): 892-895, 2010.

28- HOFFMAN O. and WEBER J.R.: Pathophysiology and treatment of bacterial meningitis. Ther. Adv. Neurol. Disorder, 2 (6): 401-412, 2009.

29- EL-KAPANY R.A.: Serum and CSF Cortisol Level in Patients with Meningitis. Egypt J. Neurol. Psychiatry Neurosurgery, 48 (4): 391-397, 2011.

30- ALAM A., MORAD W., BAHBAH M., et al.: Epidemiological and clinical study of bacterial meningitis in Menofia governorate. Journal of medical science and clinical research, Volume (1) Issue (3). pages 130-140, 2013.

31- DASTYCH M., GOTTWALDOVA J. and CERMAKOVA Z.: Calprotectin and lactoferrin in CSF; Biomarkers utilizable for differential diagnostics of bacterial and aseptic meningitis. Clinical Chemistry and Lab Med., 53 (4): 599-603, 2015.

32- DHAS D., BHAT B. and GANE D.: Role of calprotectin in infection and inflammation. Biology. Current Pediatric Research, 16 (2): 83-94, 2012.

فائدة قياس الكالبروتكتين فى السائل الدماغى النخاغى فى إلتهاب السحايا الحاد

إلتهاب السحايا هو إلتهاب الأغشية الواقية التى تغطى الدماغ والنخاع الشوكى. وقد يمكن أن يكون إلتهاب السحايا الحاد حالة مهددة للحياة بسبب قرب الإلتهاب من الدماغ والحبل الشوكى. لذلك كانت إجراءات التشخيص الفورى مطلوبة للتمييز بين إلتهاب السحايا البكتيرى وإلتهاب السحايا غير البكتيرى.

هدف الدراسة: هدفت هذه الدراسة إلى تقييم الفائدة التشخيصية لقياس مستوى كالبروتكتين فى السائل الدماغى النخاعى للتمييز بين إلتهاب السحايا البكتيرى وإلتهاب السحايا العقيم الحاد.

الطريقة: أجريت هذه الدراسة على ٦٠ حالة ظهرت عليها أعراض إلتهاب السحايا (ارتفاع فى درجة الحرارة، صداع شديد، تغير فى الحالة العقلية، تجنب الضوء الساطع وتيبس الرقبة) حيث تم عمل تحليل مختبرية للسائل الدماغى النخاغى (CSF) الموجود فى المختبر التقليدى مثل الجلوكوز والبروتين الكلى وعدد كرات الدم البيضاء، تم تقسيم هؤلاء المرضى إلى ثلاثة مجموعات الأولى ١ وتشمل ثلاثون مريضاً مصاباً بالتهاب السحايا البكتيرى، والمجموعة الثانية وتشمل ثلاثون مريضاً مصاباً بالتهاب السحايا غير البكتيرى والمجموعة الثالثة وشملت ٣٠ شخصاً من الأشخاص الذين يخضعون للتخدير النخاعى لأسباب جراحية غير عصبية كمجموعة ضابطة. تم تحديد تركيز كالبروتكتين السائل الدماغى النخاعى بواسطة ELISA فى جميع الحالات.

النتائج: كانت المستويات الأعلى من الكالبروتكتين فى السائل الدماغى لدى مرضى إلتهاب السحايا البكتيرى بمتوسط قيمة 10.2±2.36 نانو غرام/مل مقارنة بمجموعة إلتهاب السحايا غير البكتيرى حيث 8.7±1.91 نانو غرام/مل، مع وجود فرق معتد به إحصائياً وكان مستوى الكالبروتكتين فى المجموعة الضابطة أقل من المستويات فى المرضى غير المصابين بالتهاب السحايا بمتوسط قيمة 6.5±1.45 نانو غرام/مل مع فرق معتد به إحصائياً وكانت الكفاءة التشخيصية للكالبروتكتين عند التمييز بين إلتهاب السحايا البكترى وإلتهاب السحايا غير البكتيرى.

الاستنتاجات: قد يكون قياس الكالبروتكتين فى السائل الدماغى النخاغى فى تشخيصاً لالتهاب السحايا الحاد ويمكن أن يكون قياسه مفيداً فى التمييز بين إلتهاب السحايا البكتيرى وغير البكتيرى الحاد.