

## Cerebrospinal LDH and Serum Pct in Diagnosis of Meningitis

Sayed Farouk Mohammed<sup>1</sup>, Taha Hussein Singer<sup>2\*</sup>, Mahmoud Basstawy Ismail<sup>2</sup> and Nagla Abdel Moniem Radi<sup>3</sup>

<sup>1</sup>Department of Tropical Medicine, Faculty of Medicine, Al Azhar University, Egypt

<sup>2</sup>Faculty of Medicine, Fever Hospital Beni Suef, Beni Suef University, Egypt

<sup>3</sup>Faculty of Medical Microbiology and Immunology, Al Azhar University, Egypt

\*Corresponding author: Taha Hussein Singer, Faculty of Medicine, Fever Hospital Beni Suef, Beni Suef University, Egypt, Tel: 00201001926944; E-mail: tahahussien50@yahoo.com

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### Abstract

**Context:** Meningitis means the membranes that cover the brain, spinal cord and the intervening cerebrospinal fluid inflamed.

**Aims:** To assess the diagnostic role of cerebrospinal LDH and serum procalcitonin in meningitis and differentiating Septic from Aseptic meningitis.

**Settings and design:** Cases were divided into septic meningitis (Group I), Aseptic meningitis (Group II), and meningism (Group III) and 100 control cases complain other than CNS infection

**Material and methods:** Patients were evaluated by full clinical examination, laboratory investigation (CBC, ESR, CRP, & RBS, Liver and Renal function tests, and Blood culture), LP for CSF examination, Cerebrospinal LDH by Spectrophotometer, Serum PCT in selected patient, CT and MRI in complicated cases.

**Statistical analysis used:** Data were collected and statistically analyzed using: chi square ( $\chi^2$ ) test, Spearman correlation coefficient test and Mann-whitney test

**Results:** It was found that cerebrospinal LDH (100%) of 139 cases in septic meningitis and (98%) of 104 cases in Aseptic meningitis were elevated above normal range. all cases of meningism show normal range. Furthermore, S. PCT testing was positive in all patients with septic meningitis, while S. PCT testing is positive in 35 patients (34%) with Aseptic meningitis and negative in 69 patients (66%). And S. PCT-Q testing was negative in all patients with meningism. control cases were assessed as normal S. PCT level.

**Conclusion:** Cerebrospinal LDH can be used only as a preliminary screening test, whereas PCT-Q was a good diagnostic marker for distinguishing septic from aseptic meningitis.

**Keywords:** Procalcitonion; LDH; PCT; Tropical

### Key Messages

Clinical manifestation cannot be differentiated between Septic and Aseptic meningitis, So Cerebrospinal LDH can be used as a preliminary screening test, whereas PCT-Q was a good diagnostic marker for distinguishing septic from aseptic meningitis with high sensitivity and specificity.

### Introduction

The triad of fever, boring headache and projectile vomiting is suggestive of the disease [1]. The most common organism of septic meningitis is pyogenic bacteria, while viruses are the main cause of the Aseptic meningitis. Tunkel and Afifi et al. [2,3] defined Septic meningitis as one of vital cause of death worldwide, so it's considered an endemic disease in Egypt. Bannister et al. [4]. Diagnosed Septic meningitis by microscopy of a Gram stained smear, positive CSF culture, and by results of lumber puncture.

### Aim of the work

The primary objective of the present study was to assess the diagnostic role of cerebrospinal LDH serum procalcitonin in meningitis in Beni-suief governorate and for differentiating Septic from Aseptic Meningitis

### Subjects and Methods

This study was conducted at Beni-seuf Fever Hospital for two years; in the period between the first of March 2014 to 30th March 2017 this study was conducted on 260 patients with Symptoms and Signs of clinically acute Meningitis & 100 persons as a control after a written consent for each patient. Patients. Were selected from Meningitis wards in Beni-seuf Fever Hospital, Beni-seuf governate, Egypt. While control persons were selected from inpatients at other wards. and enrolled 100 control and 260 patients divided into four groups: septic meningitis (Group I) (139 patients), Aseptic meningitis (104 patients) (Group II), and meningism (Group III) (17 patients) and 100 control cases who were attending fever hospital for other complain than CNS

infection from where blood samples were taken to test S. protein S. LDH and S. procalcitonin.

## Results

A total number of 260 cases with the clinical suspicion of meningitis within 1-5 days of onset of their illness presented to outpatient clinics and Emergency Room department were admitted to Bani-seuif Fever

Hospital for whom a lumbar puncture and laboratory studies were performed at the same time to establish the diagnosis., it was evident that all the three groups followed the same seasonal variation i.e. the lowest number of cases were reported in the Winter months (January, February and March) and the largest numbers were seen in the Summer months (June, July, and August). This increased incidence of cases in each group in Summer season was highly significant ( $p < 0.0001$ ) (Table 1).

Month	Group I Septic Meningitis	Group II Aseptic Meningitis	Group III Meningism
March	4	8	0
April	7	8	1
May	9	9	1
June	36	13	3
July	29	12	5.
August	23	15	4
September	8	8	1
October	7	5	0
November	6	8	1
December	4	7	1
January	3	7	0
February	3	6	0
Total	139	104	17

**Table 1:** Monthly incidence of cases in each group of study patients.

The mean values ( $\pm$  SD) for Protein level (serum Protein and CSF Protein levels) in meningitis were shown a significant difference between studied groups was found as regard mean Protein level. So the

cut off values confirm that CSF contains exudate indicated infections (Table 2).

Variables	Groups	Group I septic Meningitis No 139	Group II Aseptic Meningitis No 104	Group III Meningism No 17	p-Value
Serum protein Level (6–8.3 ) mg/dL	Mean Value	7.3	21.6	6.8	0.001
	$\pm$ SD	0.9	46.8	0.07	
CSF protein Level (20 – 50) mg/dL	Mean Value	89.5	47	23	0.00
	$\pm$ SD	21.5	21.6	1.3	
Cut off value of CSF protein > 50 mg/dl in studied groups.					

**Table 2:** Comparison between serum protein and CSF protein regarding.

Table 3 shows the comparing results of serum LDH testing in the studied groups, it was found that 139 (100%) of 139 of cases were above normal range elevated serum LDH in septic meningitis. while 102 (98%) of 104 cases were show above normal range elevated serum

LDH, while 2 (2%) of 104 cases were show below normal range in Aseptic meningitis group. all cases of meningism show normal range. Only 2 control cases were showed S. LDH above normal and they were complained of chest infection (pneumonia).

Serum LDH (120-246 U/L)	Group I Septic Meningitis No 139		Group II A Septic Meningitis No 104		Group III Meningism No 17		Group IV Control group	
	NO	%	NO	%	NO	%	NO	%
>246	139	100	102	98	17	100	2	2
<120	0	0	2	2	0	0	98	98
Cut off of CSF LDH>0.6 U/L of Serum LDH level								

**Table 3:** Comparison between studied groups regarding serum LDH level.

The mean values ( $\pm$  SD) for LDH level (serum LDH and CSF LDH levels) in septic and aseptic meningitis were shown in Table 4.

Groups Variables		Group I Septic Meningitis No 139	Group II Aseptic Meningitis No 104	Group III Meningism No 17	p-Value
Serum LDH Normal (120-250 U/L)	Mean Value	410.5	165.1	136	0.000
	$\pm$ SD	306.9	132	134.7	
CSF. LDH Normal (0-0.6 U/L)	Mean Value	1093	78.9	41	0.000
	$\pm$ SD	2004	40.2	2.7	
Cut off of CSF LDH>0.6 U/L Of Serum LDH level					

**Table 4:** Comparison between studied groups regarding mean LDH level.

Table 5 shows the comparing results of serum PCT-Q testing in the studied groups, it was found that S. PCT testing was positive in all patients with septic meningitis while S. PCT testing is positive in 35 patients (34%) with Aseptic meningitis and negative in 69 patients

(66%). And S. PCT-Q testing was negative in all patients with meningism. Also all control cases were assessed as normal S. PCT level.

Serum Procalcitonin (0.5-2 ng/ml )	Group I Septic Meningitis No 139	Group II A Septic Meningitis No 104	Group III Meningism No 17	Group IV Control group No 100
>2 ng/ml	139	35	0	0
<0.5 ng/ml	0	69	17	100
Cut off of S. PCT>2.5 ng/dL				

**Table 5:** Comparison Between studied groups regarding serum procalcitonine level.

## Discussion

All patients who were admitted to Beni-suief fever hospital with the clinical suspicion of meningitis and who were underwent a lumbar puncture and laboratory studies at the same time were enrolled in this study. According to the discharge diagnosis, patients were classified into three diagnostic groups: septic, Aseptic meningitis and meningism. Septic Meningitis is a bacterial inflammation of the meninges and is identified by an abnormal number of white blood cells in cerebrospinal fluid [5]. The second group i.e. aseptic meningitis, is defined as meningitis in which no bacterial pathogen can be isolated by routine cultures, and a clear CSF with a leukocyte count  $\leq 100$  cell/mm<sup>3</sup> and is caused by either infectious causes (viral, bacterial and fungal infection) or noninfectious causes as autoimmune diseases and is identified by an abnormal number of lymphocytic CSF pleocytosis, the neurologic examination in this disease is normal except for

meningism [2,6]. This stratification of meningitis patients was based on the WHO case definition of septic meningitis Campagne et al. [7] and many other investigators. These references documented septic meningitis by the detection in the CSF of  $>100$  white blood cells per ml in cases of negative bacterial cultures, latex film Youssef et al. and Afifi et al. [3,8]. Meningism is usually applied to those conditions who present with meningeal symptoms but CSF examination is normal and the subsequent investigation and evolution of the disease reveal the true diagnosis e.g. pneumonia, or subarachnoid hemorrhage Bannister et al. [4].

A significant difference between studied groups was found as regard means LDH. So the cut off values confirm that LDH values increased indicated exudate and infections. Current study revealed that septic and aseptic meningitis cases were found to peak during the summer months. Several studies agree with the current study, found that septic

and aseptic meningitis cases increased during the summer months. In contrast Tawfik [9], demonstrated that winter and early spring were the seasonal peak of infection, whereas Youssef et al. [8] conducted that meningitis peaked in late Autumn and Winter months, Especially for patients with culture confirmed. This result could be attributed to increase susceptibility to meningitis which occurred by dry and dusty winds from the Sahara desert that affecting back of the nose and throat lining. the current study results also revealed that (0.6 U/L ) CSF LDH level cut off and (2.5 ug/dL) serum PCT level cut off differentiating septic from Aseptic meningitis. where, serum CSF LDH>0.6 U/L referred to septic meningitis, and serum CSF LDH below this level indicated Aseptic meningitis with a sensitivity of 98% and a specificity of 98%, several studies accordance with the current study results that (0.6 U/L ) CSF LDH level cut off was a good predictor for differentiating between septic and aseptic meningitis, as Tunkel et al. and Huy et al. [6,10] conducted that elevation of LDH level in the CSF is one of the best predictor of septic meningitis. bacterial meningitis (>6 u/l), and aseptic meningitis (<2 u/l). However Qateae et al. [11] findings were inconsistent with the findings of the current study that CSF LDH has no role in differentiation septic from aseptic meningitis. The other significant predictor for differentiating bacterial from aseptic meningitis was (2.5ug/dL) serum PCT level cut off. Whereas patients with septic meningitis had a serum PCT level>2.5 ug/dL and aseptic meningitis had a serum PCT level below this level) with a sensitivity of 100% and a specificity of 100% In accordance with the current study results, Prasad et al. [12] identify serum PCT level cut off>5 ug/dL with (sensitivity 98.3% and specificity 93.5%), Gendrel et al. [13] conducted that serum PCT level cut off>5 ug/dL with (sensitivity 94% and specificity 100%)., Inconsistent, Viallon et al. [14] with serum PCT level cut off>0.2 ug/dL with sensitivity and specificity up to 100% in the diagnosis of septic meningitis obtained. Also Dubos et al. found that a PCT used alone at a 0.5 ug/dL threshold, offered the best sensitivity (99%) and specificity (83%). Similarly, Dubos et al. [15], identified a PCT  $\geq$  0.5ug/dL and a CSF protein  $\geq$  0.5 g/L were the best biologic tests with 89% and 86% sensitivity rates, 89% and 78% specificity rates Also Kapoor et al. [16] demonstrated that cut-off level of 0.28 ug/dL with sensitivity and specificity up to 100%. Whereas Dubos et al. [17] reported that no significance of PCT level sensitivity and specificity, especially in adult populations agglutination test or direct examination of a Gram stained CSF.

Regarding the inconsistent of results about serum procalcitonin cut-off, it could be explained by the samples size variation, in addition to the influence of open sample age in the current study, Compared to studies with a restricted age. Furthermore some studies reported in languages other than English [18,19].

## Conclusion

Cerebrospinal LDH can be used only as a preliminary screening test, whereas PCT-Q was a good diagnostic marker for distinguishing septic from aseptic meningitis with high sensitivity and specificity. These data should be confirmed in further study.

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