



RESEARCH ARTICLE

# The investigation of the efficiency of leukocyte esterase strip test in rapid diagnosis of bacterial meningitis

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## ABSTRACT

**Introduction:** Bacterial meningitis can impose many unintended consequences in patients. As a result, rapid diagnosis and application of imperial therapy as soon as possible can reduce patients' mortality, so the purpose of present study is to investigate the efficiency of leukocyte esterase strip test in the rapid diagnosis of bacterial meningitis.

**Materials and Methods:** This study was based on a cross-sectional study. The target population was included all patients admitted to the infectious ward of the hospital with a probability diagnosis of LP meningitis. Leukocyte esterase, protein and glucose tests were evaluated in all patients and protein above 45 and glucose less than  $\frac{2}{3}$  blood concurrent glucose and positive leukocyte esterase with each number were considered as positive cases and finally sensitivity, specificity, positive predictive value and negative predictive value of these tests were evaluated.

**Results:** According to the results of the present study, 66.7% were male and 33.3% were female. 51.9% were under 60 years old and 48.1% were over 60 years old and 29.6% had fever and 70.4% had no fever. The sensitivity of urinary strip test in the diagnosis of bacterial meningitis was obtained for glucose 66.7% and for specificity 73.3% and for positive predictive value 66.7% and for negative predictive value 73.3%. Sensitivity and specificity for protein was obtained 25% and 93.3%, respectively. Also, sensitivity and specificity for leukocyte esterase was obtained 50% and 100%, respectively.

**Conclusion:** According to the results, the specificity and positive predictive value of leukocyte esterase were obtained very excellent in differentiating bacterial meningitis and the sensitivity was not in an optimal extent. It is suggested that leukocyte esterase be used as an early and rapid diagnostic test along with glucose and protein to aid in imperial therapy by clinicians.

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## KEYWORDS:

Meningitis, Leukocyte esterase, Strip test.

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## INTRODUCTION

Throughout the history, infectious diseases had an direct relationship with human health. The evolutionary effects of infectious diseases are dramatic with the involvement of the human immune system and to a lesser extent, its genetic makeup (1). Among the 59 million deaths that occur each

year worldwide, more than a quarter of it is due to infectious diseases (2). Bacterial meningitis is an acute purulent infection of the leptomenigeal that is one of the most common infectious diseases in children so that the mortality rate in this disease is still very high (3). This disease is considered as a major disease in the world. Bacterial meningitis is associated with an inflammatory reaction of the

CNS that may cause decrease of consciousness level, seizures, increased intracranial pressure (ICP), stroke, and nervous sequelae (4).

This disease is the most common form of purulent CNS infection and its annual incidence amount in the United States is more than 2.5 cases per 100,000 people. The organisms that are the most common causes of bacterial meningitis in the community are as follow: *Streptococcus pneumoniae* (50%), *Neisseria meningitis* (25%), group B streptococci (15%) and *Listeria monocytogenes* (10%) (5). The risk factors creating bacterial meningitis are as follow: Recent colonization of bacterial pathogens, population, poverty, black race, male gender and possibly non-breastfeeding for infants 2-5 months. Streptococcal meningitis is also considered as a complication of diagnostic myelography (6, 7).

An observational study showed that approximately 4,000 cases of bacterial meningitis and 500 cases of death were occurred annually between 2003 and 2007 (8). Early diagnosis and treatment of this disease has many importance in reducing complications and inexpensive rapid diagnostic tests can be very helpful because acute infections of the nervous system are one of the most important issues in medicine and early diagnosis, effective decision-making and rapid initiation of treatment can be the saver life of the patient and according to the necessity for a test-taking which helps to a faster diagnosis and is available, performing this method will many help to achieve this goal. (9, 10). The urine test strip can be commonly used, are mostly applicable for rapid CSF analysis. Implementing this method in rural and low-income areas are very useful. It also reduces therapeutic delays even in centers where facilities are available (11). However, it is necessary that this test should be used as an attachment test for rapid screening and should not replace CSF cell and chemical testing (12, 13).

Therefore, regarding to the importance of this issue, we were decided to perform this study by investigating the efficiency of leukocyte esterase strip test in the rapid diagnosis of bacterial meningitis.

## MATERIALS AND METHODS

This study was based on a cross-sectional study. The target population was included all patients admitted to the infectious ward of Valiasr Hospital in Zanjan, Iran, who were diagnosed with LP (Lumbar Puncture) meningitis in June 2017 to June 2016. Methods and tools of data collection were included a questionnaire and the patients who had inclusion and exclusion criteria were included into the study.

## Inclusion criteria are included

all patients with possible diagnosis of LP meningitis and having informed consent and exclusion criteria are also included: the patients who have not had a successful LP.

## Sample Size Determination:

The number of 27 patients with suspected symptoms of bacterial meningitis, who were admitted in the infectious ward of the hospital during one year and had removed their spinal fluid.

## Executive Procedure:

At first, demographic information of patients including age, gender, antibiotic use were recorded. Then, the questionnaire completion was performed over the records of patients with bacterial meningitis admitted to the infectious ward of the hospital. After collecting information, we were analyzed the data and prepared a statistical table.

## Data Analysis:

The data analysis was performed using frequency distribution tables and charts drawing. Also, the sensitivity and specificity of this test were determined according to the number of leukocyte, protein and glucose.

## Ethical Considerations:

Obtaining a written introduction letter was received on behalf of the esteemed officials of the university to introduce it to the research centers. Obtaining a written introduction letter was received on behalf of the esteemed officials of the selected researcher centers. The purpose of the study was described for all research units and written consent was taken from them. The information of all patients is kept confidential by the project manager. In all stages of the research, all ethics statements in Helsinki research and ethics research committees of the University of Medical Sciences were considered. This plan was carried out after approval by the research council of the medical school and receiving the ethic Code with the number IR.ZUMS.REC.2019.387 and receiving an introduction letter was approved.

## RESULTS

In this research, a total of 27 patients were included into the study, which among these, 18 patients were male (66.7%) and 9 patients were female (33.3%). About 14 patients (51.9%) were under 60 years old and 13 patients (48.1%) were over 60 years old.

In Table 1, the basic characteristics of the studied population were investigated and the results showed that among 27 patients, 17 patients (63%) had higher white blood cell than allowable limit.

**Table 1:** Basic characteristics of the target population

Variable	Class	Percentage (Frequency)
Fever status	Has	8 (29.6%)
	Has not	19 (70.4%)
History of antibiotic use	Has	7 (25.9%)
	Has not	20 (74.1%)
Leukocytosis	Has	17 (63%)
	Has not	10 (37%)
Polymofonucleosis	Has	15 (55.6%)
	Has not	12 (44.4%)
Glucose	Has	12 (44.4%)
	Has not	15 (55.6%)
Protein	Has	4 (14.8%)
	Has not	23 (85.2%)
Leukocytostrase	Has	6 (22.2%)
	Has not	21 (78.8%)
Meningitis	Has	12 (44.4%)
	Has not	

Sensitivity, specificity, positive and negative predictive value of CSF glucose in differentiating bacterial meningitis were investigated in Table 2 and the results showed that in people under 60 years of age, 71.4% of their CSF glucose was positive

and in people over 60 years of age, 60% of their CSF glucose was positive but in total the sensitivity of this test was obtained for glucose 66.75%, for specificity 73.3%, positive predictive value 66.7% and negative predictive value 73.3%.

**Table 2:** Sensitivity, specificity, positive predictive value, negative predictive value of CSF glucose in differentiating bacterial meningitis

Population	Sensitivity	Specificity	Positive Value	Predictive	Negative Value	Predictive
Total	66.7%	73.3%	66.7%		73.3%	
Men	66.6%	71.4%	77.8%		55.6%	
Women	100%	75%	33.3%		100%	
People under 60 year	71.4%	71.4%	71.4%		71.4%	
People over 60 years	60%	75%	60%		75%	
Without fever	66.7%	80%	75%		72.7%	
With fever	66.7%	60%	50%		75%	
History of antibiotic use	100%	50%	60%		100%	
Without history of antibiotic use	55.6%	81.8%	71.4%		69.2%	

In Table (3), the sensitivity, specificity, positive predictive value, and negative predictive value of CSF protein in differentiating bacterial meningitis were investigated and the results showed that specificity (100%) and positive predictive

value (100%) were performed better for men than women and in general sensitivity (25%), specificity (93.3%), positive predictive value (75%) and negative predictive value was considered and showed that 75% of patients who their test was positive are actually sick.

**Table 3:** Sensitivity, specificity, positive predictive value, negative predictive value of CSF protein in differentiating bacterial meningitis

Population	Sensitivity	Specificity	Positive Value	Predictive	Negative Value	Predictive
Total	25%	93.3%	75%		60.9%	
Men	18.2%	100%	100%		43.8%	
Women	100%	87.55	50%		100%	
People under 60 year	42.9%	100%	55%		63.6%	
People over 60 years and above	100%	87.55	100%		58.3%	

Without fever	22.2%	100%	100%	58.8%
With fever	33.35	80%	50%	66.7%
History of antibiotic use	66.7%	75%	66.7%	75%
Without history of antibiotic use	11.1%	100%	100%	57.9%

The results of Table 4 show that leukocyte esterase has very accurate in identifying healthy individuals so that in healthy individuals, positive cases cannot be expected to be reported.

**Table 4:** Sensitivity, specificity, positive predictive value, negative predictive value of CSF leukocyte esterase in differentiating bacterial meningitis

Population	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Total	50%	100%	100%	71.4%
Men	45.5%	100%	100%	53.8%
Women	100%	100%	100%	100%
People under 60 year	71.4%	100%	100%	77.8%
People over 60 years and above	100%	20%	100%	66.7%
Without fever	33.35	100%	100%	62.5%
With fever	100%	100%	100%	100%
History of antibiotic use	66.7%	100%	100%	80%
Without history of antibiotic use	44.4%	100%	100%	68.8%

## DISCUSSION

In the developed countries, bacterial meningitis is a purulent infection in the subarachnoid space with an annual prevalence of 2-6 per thousand adults and a mortality rate of more than 88% (14). The outcome of bacterial meningitis largely depends on the early initiation of appropriate antibiotic treatment. Various biochemical markers have been used for the early diagnosis of bacterial meningitis such as lactate, LDH, CRP, ferritin and cytokines (15). The most sensitive aspect in the pathogenesis of bacterial meningitis is the effect of general immunity against infectious agents in the central nervous system (CNS). Bacteria proliferate in the CNS and release pathogen-associated molecules such as lipopolysaccharides, peptidoglycans, and nucleic acids, which this process lead to activate resident macrophages, astrocytes, and microglia via Toll-like receptor and eventually causes to produce Cytokines. (16). Therefore, the purpose of present study is to evaluate the diagnostic value of leukocyte esterase, protein and glucose in CSF in order to diagnose bacterial meningitis. The results of the present study showed that the sensitivity of this test was obtained for glucose about 66.75%, for specificity 73.3%, for positive predictive value 66.7% and for negative predictive value 73.3%. In a study by DeLozier et al. (17) reported leukocyte

esterase sensitivity for the diagnosis of bacterial meningitis proven by CSF culture of 73% and 95%, respectively, while the sensitivity of this test in the present study was obtained lower than the DeLozier study. The specificity in this study was slightly higher (100%) compared to 95% in the DeLozier study. These results show that leukocyte esterase is very accurate in identifying healthy individuals so that positive cases cannot be expected to be reported in healthy individuals. Also in the present study, positive predictive value was obtained 100%, which shows that if the test is positive, it can be said with certainty that the patient has bacterial meningitis. However, sensitivity of 50% will cause relying solely on this test to prevent 50% of patients from being diagnosed with bacterial meningitis

In a study by Shokouhi et al. (18) reported leukocyte esterase sensitivity and specificity for 84.6% and 94.5%, respectively. In this study, although the specificity of this test was comparable with the results of this study (94 vs. 100), but the sensitivity of the test was obtained 84.6%. Some differences in the studies' results can be attributed to differences in study populations, types of bacterial and non-bacterial meningitis that were examined in different studies. In addition, the cut points for the indicators studied in different studies, based on laboratory references can play a role in these differences.

Archana Bhat et al. (19) reported leukocyte esterase sensitivity and specificity of 36.36% and 85.71%, respectively. So that sensitivity and specificity in Archana Bhat study were obtained about 15% less on average than the present study. In Joshi study (20) for leukocyte esterase test, sensitivity and specificity of 85.2 and 89.6% have been reported. In this study, as it was mentioned, the level of cerebrospinal fluid protein in the diagnosis of bacterial meningitis was investigated and the sensitivity and specificity were obtained 25% and 93.3%, respectively.

In the study by Archana Bhat et al. (19) in 2018, the sensitivity and specificity were obtained 100% and 28.57%, respectively, which is in complete contradiction with the results of the present study. This issue can be attributed to the selection of the cut-off point for the Prot above CSF, while in this study the protein level above 45 per deciliter was considered as the cut-off point, in the Bhat study the number 30 was chosen as the cut-off point. The lower cut-off point will cause more patients to be identified if they are ill which as a result the high sensitivity is obtained. However, this high sensitivity will finish due to the selection of a low cut-off point result in cost of reducing the specificity so that many healthy people will be falsely considered as patients. This subject increases the number of false positive cases and thus reduces the sensitivity and specificity of the test.

By selecting a cut-off point of 45 in the present study, it is possible that many patients with protein below 45 are in the category of healthy individuals, and as a result, the sensitivity of the test to identify patients is reduced, or on the other hand, selecting this high cut-off point causes Healthy people will be less likely to be mistaken for a patient, meaning a lower false positive will result in a higher specificity. In this study, CSF glucose level was also investigated in the diagnosis of bacterial meningitis, which the sensitivity and specificity were obtained 66.7% and 73.3%, respectively. In the Enshogopta study (21) in 2017 with the aim of rapid analysis of CSF with urine reagent strips in meningitis cases, the amount of sensitivity 98.13% and specificity of 31.92% for glucose were reported, which was approximately 20% higher than the present study.

In this study, it was shown that leukocyte esterase test with 100% specificity and 100% positive predictive value can be useful in differentiating bacterial meningitis from other meningitis. This can help clinicians which perform empirical treatment with more confidence in people who their test is positive. However, the low sensitivity of this test (50%) means that relying solely on this test will prevent almost half of the patients who are actually ill not being identified as patients. Also, the sensitivity, specificity, positive predictive value and negative predictive value for glucose in the present study were relatively favorable limit. However, in the present study it suffers from some limitations. One of the limitations in this study is the low sample size, which can reduce the generalizability of the study results. This volume of low sample was created, although in the results section of

subgroup analyzes based on the predicted goals, age, gender, fever and antibiotic use are conducted but, however, these results could not be interpreted for comparison with other studies.

## CONCLUSION

While the specificity and positive predictive value of leukocyte esterase were obtained very excellent in differentiating bacterial meningitis, the sensitivity was not in an optimal limit. In this study, for protein, while the sensitivity was very low, but the specificity of the test was desirable. In general, the use of glucose and protein along with leukocyte esterase can be more effective in clinical decisions than leukocyte esterase alone. It is suggested that leukocyte esterase to be used as an early and rapid diagnostic test along with glucose and protein to aid in imperial treatments by clinicians.

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