
ORIGINAL ARTICLE**Role of urine reagent strips in early diagnosis of meningitis***Preeti Singh¹, Vijay Kumar Jaiswal², Neha Singh¹, Anamika Singh Thakur^{3*}*

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Abstract

Background: Early diagnosis of meningitis is critical to reducing associated morbidity and mortality, especially in resource-limited settings. Conventional Cerebrospinal Fluid (CSF) analysis is accurate but time-consuming. Urine reagent strips offer a rapid, bedside alternative for detecting key CSF abnormalities. *Aim and Objectives:* To evaluate the diagnostic accuracy of urine reagent strips (Combur 10 Test M, Roche, Germany) in detecting CSF leukocytes, glucose, and protein in patients with suspected meningitis. *Material and Methods:* This prospective study included 100 CSF samples from patients aged 0 to 62 years, clinically suspected of meningitis and admitted to LLRM Medical College, Meerut, between January and December 2022. CSF samples were simultaneously analyzed using standard cytochemical methods (gold standard) and urine reagent strips. Diagnostic performance was assessed using sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and accuracy. *Results:* Of 100 patients, 75% were children, 40% of whom were neonates. Diagnosed cases were tubercular meningitis (68%), bacterial meningitis (20%), aseptic meningitis (9%), and normal CSF (3%). The urine reagent strips had high diagnostic accuracy: leukocytes: showed sensitivity 100%, specificity 97%, accuracy 98%. Glucose had a sensitivity 97.4%, specificity 95.6%, accuracy 97% while protein had sensitivity 98.5%, specificity 79.3%, accuracy 93%. *Conclusion:* Urine reagent strip method is a fast, effective screening test for initial CSF analysis in suspected meningitis. The ease of use, short turnaround time, and high reliability are particularly beneficial in emergency or resource-limited settings, allowing for expedient clinical decision-making.

Keywords: Meningitis, cerebrospinal fluid, urine reagent strips, Combur 10 Test, rapid diagnosis

Introduction

Bacterial meningitis, an intracerebral and intraspinal infection, requires timely diagnosis to prevent potentially severe neurological impairment or mortality [1, 2]. It is dependent upon the analysis of Cerebrospinal Fluid (CSF). Diagnostic confirmation most commonly involves cell count in cerebrospinal fluid, measurement of glucose and protein levels, and microbiologic study—all procedures which require exposure to a sophisticated laboratory and staff familiar with performance—usually at

a cost that necessitates protracted turnaround times [3].

In past research, urine reagent strips have been investigated as an analyte for CSF examination, but they have not gained widespread use. The strips present the possibility for rapid bedside measurement of CSF parameters like glucose, protein, and leukocyte count, which can be particularly helpful in cases of medical emergency when instant treatment decisions are paramount

[3-8]. This research aimed to evaluate the diagnostic validity of urine reagent strip as a point-of-care tool for early detection of meningitis, especially in conditions where early diagnosis is crucial to begin proper therapy. Current study is proposed to estimate the diagnostic validity of urinary reagent strip in early diagnosis of meningitis as a bedside test, where rapid diagnosis is necessary for earliest treatment needed for patient. In our study, we compared the outcomes of reagent strip test with biochemistry and microscopy to see how precise and useful reagent strip testing is in detecting CSF proteins, glucose and leucocytes.

Material and Methods

This prospective study was done on patient admitted the Department of Medicine Sardar Vallabh Bhai Patel Hospital and LLRM Medical College, Meerut, with clinical suspicion of meningitis. One-hundred patients were enrolled over the period of one year (Jan 2022 to Dec 2022). Institutional Ethics Committee approval was obtained, and informed consent was given by all study participants. Cerebrospinal fluid samples in these clinically suspected meningitis cases were received at the Department of Pathology within one hour after lumbar puncture, after they had been collected in the Medicine and Pediatrics Departments.

The sample size was calculated based on the number of patients attending the pediatric unit with symptoms of meningitis during the study duration.

Inclusion Criteria: Patients of any age (from birth until 62 years old) with suspected meningitis and symptoms of abrupt high-grade fever, stiff neck, headache, nausea or vomiting, and confusion or difficulty in concentrating [9] with sufficient CSF samples were included.

Exclusion Criteria: CSF samples that were hemorrhagic or not enough in number were not included in the study.

CSF was aspirated by lumbar puncture, and laboratory testing was carried out within an hour of the sample being drawn. Initial screening was done using the Combur 10 Test M strip (Roche, Germany). A pipette was used to apply 2–3 drops of undiluted CSF on the test patches for protein, glucose, and leukocyte esterase. Changes in color were noted and results interpreted according to the manufacturer's color scale. Reagent strips can measure leukocyte count from 10 to 500 cells/mm³ based on leukocyte esterase activity.

Definitive test: were performed by- cell count by Neubeauer's chamber with differential count on centrifuged smears, stained with Leishman stain. Protein and sugar estimation was carried out by standard biochemical method.

Normal CSF values employed were leucocytes: 0-5 cells/ μ l (adults) and 0-30 cells / μ l (neonates), Glucose :50-80 mg/dl and proteins:15-45 mg/dl. (Table 1)

Leukocyte reagent strip vs. microscopic examination

No color on the strip equates to < 10 leukocyte/mm³, i.e., a normal or non-inflammatory condition; 1+ color change equates to 10–75 leukocyte/mm³, i.e., mild increase in white blood cells– possible early or mild infection; 2+ equates to 75–500 leukocytes/mm³, i.e., moderate infection or inflammation; 3+ matches > 500 leukocytes/mm³, indicative of severe infection or severe inflammatory process.

Glucose reagent strip vs. biochemical value

No color suggests < 50 mg/dL glucose, found in bacterial meningitis or any other situation when glucose is metabolized by infectious agents or cells of the immune system; 1+ corresponds to 50–100 mg/dL, slightly low glucose; 2+ is equivalent to 100–300 mg/dL, near or just higher than normal range; 3+ equates to 300–1000 mg/dL; and 4+ reflects > 1000 mg/dL, typically not physiological for CSF and may reflect contamination or testing error if in CSF context (this range is more relevant for urine).

Protein reagent strip vs. biochemical value

No color means < 30 mg/dL, within normal CSF protein levels; 1+ corresponds to 30–100 mg/dL, indicating mild protein elevation—possibly early infection or inflammation; 2+ matches 100–500 mg/dL, suggesting significant protein elevation, commonly seen in infections or blood-CSF barrier disruption

Statistical analysis

XLSTAT software was used to calculate sample size. The diagnostic accuracy of the reagent strip versus the standard (gold standard test) was

estimated. Sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were calculated and *p* value was derived by Chi-square test and Fischer's exact test.

Results

The study was conducted on 100 consecutive samples. Males and females contributed almost equally with 48% and 52% respectively. Majority (75%) cases were of pediatric age group <16 years) and rest 25% of cases were adults. Forty percent of cases were neonates (Table 2). In the present study, Combur 10 urinary reagent strip was used for rapid analysis of the CSF in emergency laboratory for leukocytes, proteins and glucose. Maximum cases were of tubercular meningitis 68%, with bacterial 20%, and aseptic 9%. Three percent of the samples were found to be normal. We found raised protein with increased leukocytes count in most of the cases of meningitis. Our study showed 98.5% sensitivity and 79.3% specificity for protein, 97.4% sensitivity and 95.6% specificity for sugar, and 100% sensitivity and 97% specificity for leukocytes (Table 4).

Table 1: Study parameters with Index test values and their corresponding biochemical values and microscopy

Index Test	Gold Standard	Normal Value
Leucocyte reagent strip	Microscopic examination	<5 leucocyte esterase estimation
No color	<10 leucocytes/mm ³	
1+	10-75 leucocytes/mm ³	
2+	75-500 leucocytes/mm ³	
3+	>500 leucocytes/mm ³	
Glucose reagent strip	Biochemistry value	50-80 mg/dl glucose oxidase peroxidase method
No color	<50 mg/dl	
1+	50-100	
2+	100-300	
3+	300-1000	
4+	>1000	
Protein reagent strip test	Biochemistry value	15-45 mg/dl Protein error of PH indicator
No color	<30 mg/dl	
1+	30-100	
2+	100-500	
3+	>500	

Table 2: Age wise and sex wise distribution of cases

Age	Male (%)	Female (%)	Total (%)
0 days-1 month	13	27	40 (40)
2 months -1 year	20	04	24 (24)
2 year-5 years	05	01	06 (06)
6-15 years	03	02	05 (05)
>16 years (upto 62 years)	07	18	25 (25)
	48 (48)	52 (52)	100

Table 3: Interpretation of CSF samples

	Appearance	Glucose (mg/dl)	Protein (mg/dl)	Leucocytes (cells/cumm)	Type
Normal	Clear	40-70	15-45	0-5	CSF lymphocytosis
Bacterial meningitis	Turbid	<40	100-500	>500	Polymorphonucleocytosis
Tuberculous meningitis	Slightly opaque/ cob-web form	<40	50-300	100-600	Lymphocytosis or mixed
Aseptic meningitis	Clear	Normal	Normal to mild increased	5-300	Lymphocytosis

Table 4: Diagnostic accuracy of urinary reagent strip

	Leucocyte	Glucose	Protein
True positive	34	75	70
False positive	02	01	06
True negative	64	22	23
False negative	00	02	01
Sensitivity	100	97.4	98.5
Specificity	97	95.6	79.3
Positive predictive value (PPV)	94.4	98.6	92.1
Negative predictive value (NPV)	100	91.6	95.8

Discussion

Meningitis is characterized by inflammation of the leptomeninges and is linked to high mortality rates and long-term neurological consequences due to damage to the nervous system. Delayed treatment of meningitis in neonates and infants can result in serious future impairments, including issues with language, motor function, cognition, vision,

hearing, and behavior [10]. Delayed treatment of meningitis in neonates and infants can result in long-term challenges, including impairments in language, motor skills, cognition, vision [11-12]. The definitive diagnosis greatly depends on the estimate of CSF WBC count with glucose and protein levels of CSF [13].

Chinkannaiah *et al.* utilized urinary strips for the semi-quantitative analysis of CSF cellularity and chemistry, finding high sensitivity (96.6%) and specificity (94.5%) for leukocyte estimation. The strip demonstrated a sensitivity of 96% and specificity of 87.1% for protein at a cutoff of > 100 mg/dL, while it showed lower specificity at a cutoff of > 30 mg/dL. For glucose, the strip exhibited 100% specificity, but lower sensitivity at both <40 mg/dL and < 50 mg/dL cutoffs. Our study shows the same results [3].

Parmer *et al.* in their study of 63 cases observed an overall sensitivity, specificity, PPV and NPV of 97%, 96%, 97% and 96% respectively. These findings are in correlation with our study [5].

Joshi *et al.* conducted a similar study using reagent strips and found a sensitivity of 85.2% and specificity of 89.6% for leukocytes >10 cells/cumm. For protein detection, at a cutoff of >30 mg/dL, the sensitivity was high (98.1%), but specificity was low (57.1%). However, at a cutoff of >100 mg/dL, both sensitivity and specificity were within acceptable ranges. For glucose analysis, at a cutoff of <40 mg/dL, the strip showed a specificity of 96.5% and sensitivity of 61.1%. Even at a cutoff of <50 mg/dL, the test maintained high specificity (98%) but had a lower sensitivity (46.2%) [4].

Romanelli *et al.* compared the results of reagent strips and those of the standard cytological and biochemical assays and obtained values for sensitivity, specificity, PPV, NPV and diagnostic accuracy of 91%, 98%, 95%, 96%, and 96% respectively [14].

A Gupta *et al.* conducted a similar study using the Combur reagent strip on 360 cases, finding a sensitivity of 100% and specificity of 96% for

leukocytes >10 cells/cumm. For protein detection, the sensitivity was high at 90%, but specificity was low at 54%. In terms of glucose, the strip demonstrated both high sensitivity (98%) and specificity (92%). The lower cutoff for proteins in urine was 30 mg/dL, and for CSF, it was 15 mg/dL, which can lead to false positive results, showing 1+ on the reagent strip even when CSF protein levels are within the normal range (15-45 mg/dL). This may explain the low specificity for protein in this study [15].

In the study by Mazumder *et al.*, CSF samples were analyzed using the Combur 10 urinary reagent strip for rapid assessment, followed by definitive tests. The results showed a sensitivity of 89.28% and specificity of 98.61% for leukocytes > 15 cells/cumm, and a sensitivity of 85.71% and specificity of 95.65% for CSF proteins > 30 mg/dL. For glucose levels < 50 mg/dL, the sensitivity was 48.2% and specificity was 100%. The study also found that the accuracy of the tests improved with higher cell and protein counts, while accuracy decreased for glucose, reaching 100% for high test results. This is significant, as bacterial meningitis typically presents with high CSF cell and protein levels and low glucose, distinguishing it from aseptic meningitis. The study reported 11 false negative cases (< 30 mg/dL according to the strip method), 10 of which had laboratory protein values < 45 mg/dL, the standard biochemical cutoff for normal CSF protein levels [16].

Abhirami *et al.* (2020) evaluated the Dinu H10 urine reagent strip to assess three key CSF parameters: leukocytes, protein, and glucose, comparing the results to those of the reference standard. For leukocyte counts >15 cells/cumm,

the reagent strip demonstrated a sensitivity of 92% and a specificity of 98.66%, with an overall accuracy of 97%, which improved to 100% with higher cell count cutoffs. For protein levels > 30 mg/dL, the strip showed a sensitivity of 84.33% and a specificity of 94.11%. When the protein cutoff was raised to > 300 mg/dL, both sensitivity and specificity reached 100% [17].

Bhat *et al.* assessed the diagnostic accuracy of key indicator tests using reagent strip testing as the index test, comparing the results with CSF microscopy and biochemical laboratory values (CSF proteins and glucose) as the reference standard. The reagent strip for leukocyte esterase showed a sensitivity of 36.36% and a specificity of 85.71% in detecting CSF granulocytes > 10 cells/mm³. For protein detection, the reagent strip demonstrated a high sensitivity of 100% for CSF protein levels >30 mg/dL, though its specificity was relatively low at 28.57% [18] (Table 5).

The sole minor drawback of the technique is the slight difference between normal cut-off points for sugar and protein compared to urine. High levels of

leucocyte esterase and protein in the reagent strip were determined to be equivalent to a higher leucocyte and protein concentration. This drawback can be overcome by creating strips specifically designed for CSF testing. Because the leucocyte esterase patch mainly tests for granulocytes, it is not a sensitive test for diagnosing aseptic meningitis.

Conclusion

Urine reagent strip testing of CSF for protein, glucose, and leukocytes has been promising as a quick, point-of-care diagnostic test when combined with clinical evaluation and CSF appearance. Increased cutoff values enhance diagnostic sensitivity and specificity. While larger studies are required to establish accuracy, existing evidence favors their use as a convenient substitute for conventional methods. This approach supports early bedside diagnosis of bacterial meningitis, excludes it in febrile convulsions, and supports decision-making in resource-poor situations.

References

1. Kumar A, Debata PK, Ranjan A, Gaind R. The role and reliability of rapid bedside diagnostic test in early diagnosis and treatment of bacterial meningitis. *Indian JPediatr* 2015; 82(4):311-314.
2. Scarborough M, Thwaites GE. The diagnosis and management of acute bacterial meningitis in resource-poor settings. *Lancet Neurol* 2008;7(7): 637-648.
3. Chikkannaiah P, Benachinmardi KK, Srinivasamurthy V. Semi-quantitative analysis of cerebrospinal fluid chemistry and cellularity using urinary reagent strip: An aid to rapid diagnosis of meningitis. *Neurol India* 2016; 64(1):50-55.
4. Joshi D, Kundana K, Puranik A, Joshi R. Diagnostic accuracy of urinary reagent strip to determine cerebrospinal fluid chemistry and cellularity. *J Neurosci Rural Pract* 2013; 4(2):140-145.
5. Parmar RC, Warke S, Sira P, Kamat JR. Rapid diagnosis of meningitis using reagent strips. *Indian J Med Sci* 2004;58(2):62-66.
6. Molyneux E. Where there is no laboratory, a urine patch test helps diagnose meningitis. *J Neurosci Rural Pract* 2013;4(2):117-118.
7. Oses Salvador JM, Zarallo Cortés L, Cardesa García JJ. Usefulness of reactive strips in the diagnosis of suppurative meningitis, at the patient's bedside. *An Esp Pediatr* 1988;29(2):105-108.

8. Moosa AA, Quortum HA, Ibrahim MD. Rapid diagnosis of bacterial meningitis with reagent strips. *Lancet* 1995; 345(8960):1290-1291.
9. Gupta S, Vernekar JA, Amate SS, Cacodcar JA, Vernekar AJ. Role of magnetic resonance imaging in intracranial infections at a tertiary level medical college. *JKrishna Inst Med Sci Univ* 2016; 5(2):35-48.
10. Ray P, Badarou-Acossi G, Viallon A, Boutoille D, Arthaud M, Trystram D, et al. Accuracy of the cerebrospinal fluid results to differentiate bacterial from non bacterial meningitis, in case of negative gram-stained smear. *Am J Emerg Med* 2007; 25(2):179-184.
11. de Louvois J, Halket S, Harvey D. Effect of meningitis in infancy on school-leaving examination results. *Arch Dis Child* 2007; 92(11): 959-962.
12. Krebs VL, Costa GA. Clinical outcome of neonatal bacterial meningitis according to birth weight. *Arq Neuropsiquiatr* 2007;65(4B):1149-1153.
13. Chaudhuri A, Martinez-Martin P, Kennedy PG, Andrew Seaton R, Portegies P, et al; EFNS Task Force. EFNS guideline on the management of community-acquired bacterial meningitis: report of an EFNS Task Force on acute bacterial meningitis in older children and adults. *Eur J Neurol* 2008;15(7):649-659.
14. Romanelli RM, Thome EE, Duarte FM, Gomes RS, Camargos PA, Freire HB. Diagnosis of meningitis with reagent strips. *JPediatr (Rio J)* 2001;77(3):203-8.
15. Gupta A, Dwivedi T. Reagent strips test: A simplified method for prompt analysis of cerebrospinal fluid in neurological disorders in emergency. *Pract Lab Med* 2019;16:e00124.
16. Mazumder S, Ramya BS, Biligi DS. Utility of urine reagent strips in cerebrospinal fluid analysis: An aid to bedside diagnosis of meningitis. *Indian J Pathol Microbiol* 2018;61(3):356-359.
17. Abhirami GR, Prabhu MH. Utility of urine reagent strips in CSF analysis as an aid to rapid diagnosis of meningitis. *Ann Pathol Lab Med* 2020;7(6): A-306-A-310.
18. Bhat A, Roy R, Umashankar T, Jayaprakash CS. Rapid diagnosis of bacterial meningitis by urine reagent strip testing of cerebrospinal fluid. *J Med Sci Health* 2018;4(1):15-17.

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