Section: Pathology

Original Research Article

UTILITY OF URINE REAGENT STRIPS IN BODY FLUID ANALYSIS: AN EMERGENCY WORKUP TO AID IN THE DIAGNOSIS IN RESOURCE-LIMITED SETTINGS

Sushrutha R[1], Shashank MS[2]

[1]Assistant Professor of Pathology, Sri Jayadeva Institute of Cardiovascular Science and Research, Mysuru, Karnataka, India
[2]Consultant Nephrologist, Gopala Gowda Shanthaveri Memorial Hospital, Mysuru, Karnataka, India.

Received : 07/07/2024
Received in revised form : 05/09/2024
Accepted : 20/09/2024

Keywords:
Cerebrospinal fluid, pleural fluid, ascitic fluid, synovial fluid, meningitis, spontaneous bacterial peritonitis, transudate, exudate, urinary reagent strip.

Corresponding Author:
Dr. Sushrutha R,
Email: sushusushrutha@gmail.com

DOI: 10.47009/jamp.2024.6.5.58

Source of Support :Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (5); 314-322

Abstract

Background: The gold standard for the diagnosis of meningitis, Spontaneous bacterial peritonitis (SBP), type of pleural effusion and to classify synovial fluid depends on the body fluid examination by microscopy and biochemistry which require an experienced microscopist and laboratory support. We conducted this study to determine if urinary reagent strip is useful to make a semi-quantitative assessment of protein, glucose and presence of leukocyte esterase in body fluids. The aim is to determine the chemistry and cellularity of body fluids and to correlate the parameters using urine reagent strips with routine biochemical and cytological analysis. **Materials and Methods:** This study was conducted in the Department of Pathology, HIMS, Hassan from February to July 2022. A total of 189 body fluid samples in accordance to inclusion and exclusion criteria were included in the study. Investigations for leukocytes, glucose and proteins were carried out using urine reagent strips (MISSION) and definitive test on samples by standard biochemical methods and microscopy in the clinical laboratory. We estimated the diagnostic accuracy of index test with the definitive test and constructed receiver operating curves (ROC) to evaluate overall performance of index tests and area under the curve (AUC) was estimated. **Result:** The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of leukocyte esterase positivity by strip test for body fluids was 35.4%, 100%, 100%, 81.9% and 83.6%, for the protein test was 72.4%, 93.8%, 88.7%, 83.5% and 85.2%, for cerebrospinal fluid (CSF) glucose was 100%, 4.8%, 16.9%, 100% and 20.3% respectively. ROC analysis showed that the area under the curve for urinary leukocyte strip was 0.910, for urinary protein strip was 0.861 and for glucose it was 0.524. **Conclusion:**The reagent strip test can be used to differentiate transudates from exudative effusions and infectious exudates from non-infectious exudative effusions in pleural and ascitic fluids. It is also very useful in the resource-limited settings by prompting early diagnosis of meningitis and SBP so that appropriate treatment can be initiated.

INTRODUCTION

Meningitis is a medical emergency which required to be diagnosed at earliest for proper therapeutic intervention.[1] Cerebrospinal fluid (CSF) microscopy, CSF chemistry and microbiological studies are required to make the diagnosis of meningitis. An experienced microscopist is required to estimate CSF cell count, while reasonable laboratory support is required to estimate sugar and protein levels. These facilities are often not available in resource‐limited settings, and even in settings where these are available, turnaround times are long.[2]

A pleural effusion must be characterized as transudative or exudative and, if exudative, as infectious or noninfectious. These distinctions are important for choosing the appropriate management. Examination of pleural fluid frequently provides the etiologic diagnosis.[3] Protein and leukocyte esterase in pleural fluid are of paramount importance for distinguishing transudates from exudates and for determining whether an exudate is due to an infection.[4]

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Spontaneous bacterial peritonitis (SBP) is one of the most frequent and important complications found in cirrhotic patients with ascites.[5] Polymorphonuclear count seem to be the easiest way and is faster than culture to establish the diagnosis of SBP.[6]

Analysis of synovial fluid is important for the diagnostic evaluation of patients with arthritis and joint effusion. White blood cell (WBC) count in synovial fluid allows classification of synovial fluid as non-inflammatory or inflammatory. Prompt analysis is necessary because delay may lead to false negative results.[7]

The presence of glucose, protein, leukocytes, erythrocytes and pH of a body fluid can be estimated using urinary reagent strips.

We designed this study to determine if the use of urine reagent strip to make a semi‑quantitative assessment of protein, glucose and leukocyte esterase is accurate to distinguish between a normal and an abnormal CSF, ascitic fluid, pleural fluid and synovial fluid sample. If proven useful, these strips can be an excellent test to help clinicians make a bedside rapid diagnosis of meningitis, SBP, type of pleural effusion and to classify synovial fluid so that early initiation of treatment can be done. This would greatly benefit health professionals working in resource‑limited settings.

MATERIALS AND METHODS

This study was conducted in the Department of Pathology of Hassan Institute of Medical Sciences (HIMS), Hassan from February to July 2022.Total of 189 body fluid samples i.e, CSF, pleural fluid, ascitic fluid and synovial fluid samples received in the cytology laboratory during the study period were included in the study. Insufficient quantity for performing the index test and the samples that showed obvious hemorrhagic material on gross examination were excluded from the study. Investigations for leukocyte, glucose and protein were carried out as index test by using urine reagent strips and definitive test on samples by standard biochemical methods and microscopy in the clinical laboratory. A prior approval was obtained from Institutional Ethics Committee for conducting the study.

Index test (urine reagent strip test): 10 parameter urine reagent strips of mission was used to detect cellularity (leukocyte esterase estimation), glucose (glucose oxidase‑peroxidase method) and protein levels. With the help of a pipette, 2–3 drops of undiluted body fluid was added to preexisting patches meant for protein, glucose and leukocyte estimation.

The color change was recorded and interpreted using the manufacturer provided color grading. Following was the interpretation of index test (strip reagent method, MISSION) for glucose, protein and leukocyte:

a. **Leukocytes:** The Interpretation was done after 120 seconds and depending on the color change, leukocytes were graded as:
- Negative for <15 cells/cu mm
- 1+ for 15–70 cells/cu mm
- 2+ for 70–125 cells/cu mm
- 3+ for 125–500 cells/cu mm.

b. **Proteins:** For proteins, the interpretation of the colors on the reagent strips was done after 60 seconds and were graded as:
- Negative for <15 mg/dl
- 1+ for 15–30 mg/dl
- 2+ for 30–100 mg/dl
- 3+ for 100–300 mg/dl
- 4+ for 300–2000 mg/dl

c. **Glucose:** The interpretation of the colors on the reagent strips was done after 30 seconds and were graded as:
- Negative for <100 mg/dl
- 1+ for 100–250 mg/dl
- 2+ for 250–500 mg/dl
- 3+ for 500–1000 mg/dl
- 4+ for 1000 – ≥2000 mg/dl

Definitive test for glucose and proteins were carried out by Abbott Automated Analyzer which was considered gold standard for index test. Glucose estimation was done by hexokinase method and protein estimation by biuret method. Total cell count of body fluids was calculated by microscopy using a Neubauer chamber. Differential cell count of leukocytes was carried on centrifuged smears stained by Giemsa stain.

Normal range of glucose, protein and leucocyte count in the body fluids were as follows :

CSF – Leucocytes : 0-7 cells/mm^3 in adults and 0-30 cells/mm^3 in neonates
Glucose: 45-80 mg/dl
Protein: 15-45 mg/dl

Pleural fluid – Leucocytes : 150-170 cells/cu.mm
Glucose: 70-100 mg/dl
Protein: 1-2 g/dl

Ascitic fluid – Leucocytes :<250 cells/cu.mm
Glucose: 70-100 mg/dl
Protein: 0.3-3 g/dl

The two major parameters to distinguish transudate from exudate and infectious exudates from non-infectious exudative effusions were protein and leukocyte count respectively.

Statistical Analysis: Data were entered in Microsoft Excel sheet. Sensitivity, specificity, positive predictive value, negative predictive value and the diagnostic accuracy of urine reagent strips (index test) with the microscopy and laboratory‑based measurements (reference standards) were calculated. Receiver operating curve (ROC) showing the relationship between sensitivity and specificity as a function of the strip color cut-off was plotted and area under the curve (AUC) along with its standard error was calculated using the SPSS statistical software package. Other suitable statistical tests were also applied.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

RESULTS

The study included body fluid samples of 189 patients. Of these 189 samples, 74 (39.2%) were CSF samples, 56 (29.6%) ascitic fluid, 55 (29.1%) pleural fluid and 04 (2.1%) synovial fluid samples [Figure 1].

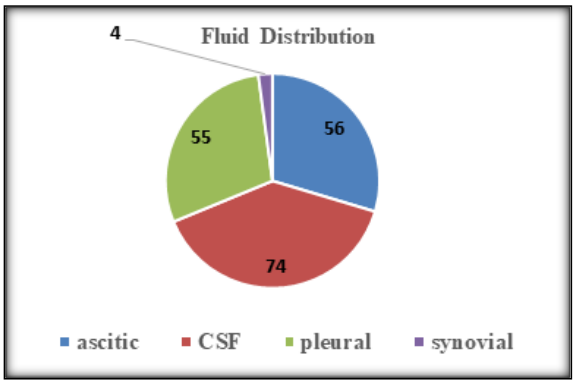

Figure 1: Fluid Distribution

Of these 189 samples, 124 appeared clear, 46 were cloudy and 19 fluid samples were turbid in appearance.

Out of 189 cases, majority of the patients were Male (n=118, 62.4%) and 71 patients were female (37.6%) [Table 1]. Median age was 42 years (range 1 day to 90 years).

CSF

The fluid sample collected from 74 patients were clinically suspected for meningitis. The maximum patients were in the age group of <1 year followed by 1-10 years. Of these 74 patients, 40 were male and 34 were female patients. The major symptoms for which patients got admitted were seizures, headache, altered sensorium and fever. Out of 74 CSF samples, 71 appeared clear and 3 samples were cloudy. Of these 74 CSF samples, 63 (85.1%) patients had normal CSF study where all the three parameters (CSF cell count, protein and glucose) were normal and in 11 (14.9%) patients the tests were abnormal and diagnosed to have meningitis.

Leukocytes

Leukocyte esterase positivity by strip test had a sensitivity of 36.4%, specificity of 100%, positive predictive value of 100%, negative predictive value of 90% and diagnostic accuracy rate of 90.5% for detection of CSF granulocytes of >15 cells/mm^3 [Table 2]. ROC analysis showed that the area under the curve for urinary leukocyte strip was 0.682 [Figure 2].

Protein

The protein positivity by reagent strip test had a sensitivity of 36.4% with specificity of 100%. Positive predictive value and negative predictive value was 100% and 90% respectively. The diagnostic accuracy rate for detection of CSF proteins was 90.5% [Table 3]. ROC analysis showed that the area under the curve for urinary protein strip was 0.682 [Figure 3].

Glucose

The glucose positivity by strip test had a sensitivity of 100%, specificity of 4.8%, positive predictive value of 16.9%, negative predictive value of 100% and diagnostic accuracy rate of 20.3%. [Table 4]. ROC analysis showed that the area under the curve for urinary glucose strip was 0.524 [Figure 4].

Pleural fluid

The fluid sample collected from 55 patients had clinical diagnosis of pleural effusion. Twelve patients had chronic obstructive pulmonary disease and 1 had acute respiratory failure. The maximum patients were in the age group of 61-70 years followed by 41-50 years. The major symptoms for which patients got admitted were breathlessness and cough. Of these 55 patients, 41 were male and 14 were female. Out of 55 pleural fluid samples,17 appeared clear, 25 samples were cloudy, 13 were turbid.Out of 55 effusions, 13 (23.6%) were transudates, 14 (25.4%) were noninfectious exudative effusions of which 10 were effusions of unknown origin, 2 were malignancies, 1 was pancreatitis, 1 was pulmonary embolism and 28 (51%) were infectious exudative effusions of which 20 were associated with tuberculosis, 6 effusions were empyema and 2 effusions were associated with pneumonia.

Leukocytes

To distinguish infectious exudates from non-infectious exudative effusions in the reagent strip, the leukocyte esterase cut off was grade 2. Leukocyte esterase positivity by strip test had a sensitivity of 28.6%, specificity of 100%, positive predictive value of 100%, negative predictive value of 57.4% and diagnostic accuracy rate of 63.6% [Table 2]. ROC analysis showed that the area under the curve for urinary leukocyte strip was 0.643 [Figure 2].

Protein

The protein level cut off to distinguish transudates from exudative effusions was 300mg/dl corresponding to grade 3 in the reagent strip. The protein positivity by reagent strip test had a sensitivity of 85.4% with specificity of 92.9%. Positive predictive value and negative predictive value was 97.2% and 68.4% respectively. The diagnostic accuracy rate for detection of proteins was 87.3% [Table 3]. ROC analysis showed that the area under the curve for urinary protein strip was 0.891 [Figure 3].

Ascitic fluid

The fluid sample were collected from 56 patients. Eight patients had chronic liver disease with portal hypertension and 2 were suspected for SBP. The maximum patients were in the age group of 41-50 years followed by 51-60 years. Of these 56 patients, 35 were male and 21 were female. The major symptoms for which patients got admitted were abdominal distension, pain abdomen and icterus. Of these 56 ascitic fluid samples, 36 appeared clear, 16

ISSN (O): 2687-5365; ISSN (P): 2753-6556

samples were cloudy, 4 were turbid.Out of 56 effusions, 36 (64.3%) were transudates, 12 (21.4%) were noninfectious exudative effusions of which 7 were effusions of unknown origin, 2 were malignancies, 2 were pancreatitis, 1 was anasarca and 8 (14.3%) were infectious exudative effusions of which 3 were associated with tuberculosis, 2 effusions had SBP of which one was culture positive and other had Culture Negative Neutrocytic Ascites (CNNA) and 3 effusions were associated with monomicrobial non-neutrocytic bacterascites.

Leukocytes

The criteria to diagnose SBP was presence of polymorphonuclear neutrophilic leukocyte (PMN) count >250 cells/mm^3 with the culture positivity in the absence of another intra-abdominal source of infection. Culture negative with PMN >250 cells/mm^3 was termed as CNNA. Monomicrobial non-neutrocytic bacterascites was defined as the presence of a single organism identified by the culture without an increased PMN count. Leukocyte esterase positivity by strip test had a sensitivity of 50%, specificity of 100%, positive predictive value of 100%, negative predictive value of 92.3% and diagnostic accuracy rate of 92.8% to distinguish infectious exudates from non-infectious exudative effusions [Table 2]. ROC analysis showed that the area under the curve for urinary leukocyte strip was 0.750 [Figure 2].

Protein

The protein positivity by reagent strip test had a sensitivity of 65% with specificity of 83.3%. Positive predictive value and negative predictive value was 68.4% and 81.1% respectively. The diagnostic accuracy rate for detection of proteins was 76.8% [Table 3]. ROC analysis showed that the area under the curve for urinary protein strip was 0.742 [Figure 3].

Glucose and pH of pleural and ascitic fluids

pH was lower in infectious exudative effusions than in transudative or noninfectious exudative effusions. Pleural and ascitic fluid glucose levels were decreased in infectious exudative effusions mainly in patients with empyema, tuberculosis and SBP.

Synovial fluid

During our study period only 04 synovial fluid samples were received with the clinical diagnosis of arthritis. Two patients were in the age group of 31-40 years, one patient each in the age group of 21-30 and 51-60 years. Of these 04 patients, 02 were male and 02 were female. The major symptom for which patients got admitted was joint pain. Out of 04 synovial fluid samples, 02 appeared cloudy and 02 were turbid.Correlation of urine reagent strip test with microscopy by Neubauer chamber was done and out of 04 cases, 03 were non-inflammatory synovial fluid and 01 was inflammatory synovial fluid sample. As the sample size was very low, we could not apply any statistical tests to find out the diagnostic accuracy of urine reagent strips for synovial fluid.

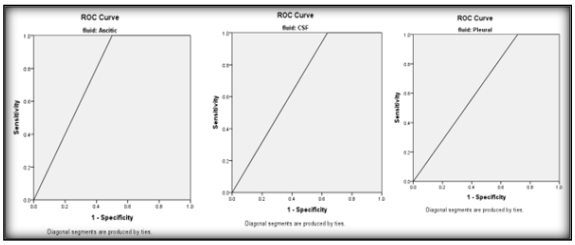

Figure 2: AUC for Leukocyte for different fluids

Area Under the Curve	
Test Result Variable(s): Leukocyte	
Fluid	**Area**
Ascitic	0.750
CSF	0.682
Pleural	0.643

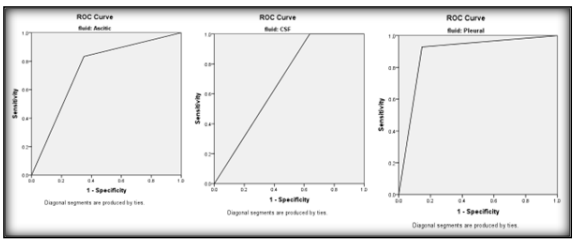

Figure 3: AUC for Protein for different fluids

Area Under the Curve	
Test Result Variable(s): Protein	
Fluid	**Area**
Ascitic	0.742
CSF	0.682
Pleural	0.891

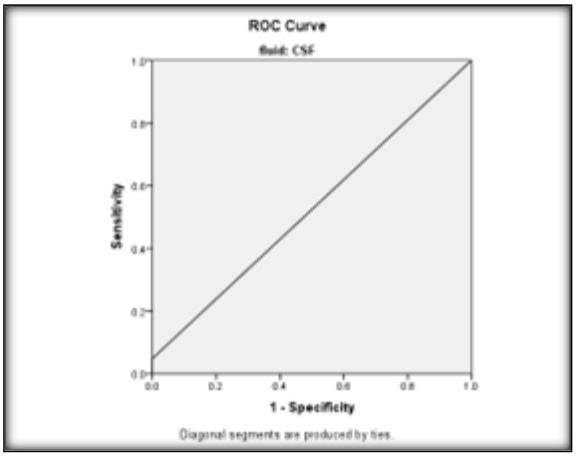

Figure 4: AUC for CSF glucose analysis

Area Under the Curve for glucose	
Fluid	**Area**
CSF	0.524

ISSN (O): 2687-5365; ISSN (P): 2753-6556

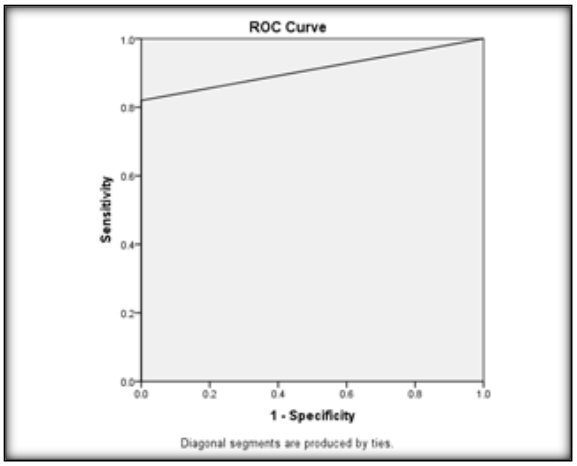

Figure 5: AUC for Leukocyte analysis of all body fluids

Area Under the Curve
Test Result Variable(s): Leukocyte
Area
0.910

Out of 189 fluid samples, there was correlation of index test leukocyte and glucose results with that of definitive test in 183(96.8%) samples. For protein the correlation of results was seen in 161(85.2%) samples.

The leukocyte esterase positivity by strip test for CSF, pleural and ascitic fluid had a sensitivity of 35.4%, specificity of 100%, positive predictive value of 100%, negative predictive value of 81.9% and diagnostic accuracy rate of 83.6%. The test result had the p value of <0.001explaining the test to be of very high significance (Table 5). ROC analysis showed that the area under the curve for urinary leukocyte strip was 0.910 [Figure 5].

The protein positivity by strip test for CSF, pleural and ascitic fluid had a sensitivity of 72.4%, specificity of 93.8%, positive predictive value of 88.7%, negative predictive value of 83.5% and diagnostic accuracy rate of 85.2%. The test result had the p value of <0.001explaining the test to be of very high significance [Table 6]. ROC analysis showed that the area under the curve for urinary protein strip was 0.861 [Figure 6].

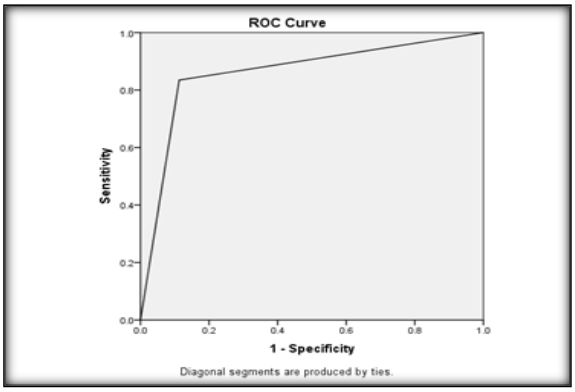

Figure 6: AUC for Protein analysis of all body fluids

Area Under the Curve
Test Result Variable(s): Protein
Area
0.861

The efficacy analysis of urine reagent strip to detect Leukocyte, Glucose and Proteins in different fluids showed low sensitivity, high specificity, high PPV with low accuracy rate. The urine reagent strip showed good specificity when the leukocyte number was high (>70 cells/cu.mm). This analysis aids in the early diagnosis during emergency.

Table 1: Gender distribution.

Gender	Number	Percentage
Male	118	62.4%
Female	71	37.6%
Total	189	100.0

Table 2: Fluid wise analysis of Leukocytes

Fluid				Positive	Negative	Total
Ascitic	Leukocyte	Positive	Count	4	0	4
			%	50.0%	0.0%	7.1%
		Negative	Count	4	48	52
			%	50.0%	100.0%	92.9%
	Total		Count	8	48	56
			%	100.0%	100.0%	100.0%
CSF	Leukocyte	Positive	Count	4	0	4
			%	36.4%	0.0%	5.4%
		Negative	Count	7	63	70
			%	63.6%	100.0%	94.6%
	Total		Count	11	63	74
			%	100.0%	100.0%	100.0%
Pleural	Leukocyte	Positive	Count	8	0	8
			%	28.6%	0.0%	14.5%
		Negative	Count	20	27	47
			%	71.4%	100.0%	85.5%
	Total		Count	28	27	55

ISSN (O): 2687-5365; ISSN (P): 2753-6556

		%	100.0%	100.0%	100.0%
a. Ascitic:Sensitivity=50%Specificity=100%Positive predictive value=100% Negative predictive value= 92.3 %Accuracy rate=92.8%					
b. CSF:Sensitivity=36.4%Specificity=100%Positive predictive value=100% Negative predictive value= 90 %Accuracy rate=90.5%					
c. Pleural:Sensitivity=28.6%Specificity=100%Positive predictive value=100% Negative predictive value= 57.4 %Accuracy rate=63.6%					

Table 3: Fluid wise analysis of Protein

Fluid				Positive	Negative	Total
Ascitic	Protein	Positive	Count	13	6	19
			%	65.0%	16.7%	33.9%
		Negative	Count	7	30	37
			%	35.0%	83.3%	66.1%
	Total		Count	20	36	56
			%	100.0%	100.0%	100.0%
CSF	Protein	Positive	Count	4	0	4
			%	36.4%	0.0%	5.4%
		Negative	Count	7	63	70
			%	63.6%	100.0%	94.6%
	Total		Count	11	63	74
			%	100.0%	100.0%	100.0%
Pleural	Protein	Positive	Count	35	1	36
			%	85.4%	7.1%	65.5%
		Negative	Count	6	13	19
			%	14.6%	92.9%	34.5%
	Total		Count	41	14	55
			%	100.0%	100.0%	100.0%
a. Ascitic:Sensitivity=65%Specificity=83.3%Positive predictive value=68.4% Negative predictive value= 81.1 %Accuracy rate=76.8%						
b. CSF: Sensitivity=36.4%Specificity=100%Positive predictive value= 100% Negative predictive value= 90%Accuracy rate=90.5%						
c. Pleural:Sensitivity=85.4%Specificity=92.9%Positive predictive value= 97.2% Negative predictive value= 68.4%Accuracy rate=87.3%						

Table 4: CSF glucose analysis

Fluid				Positive	Negative	Total
CSF	Glucose	Positive	Count	12	59	71
			%	100.0%	95.2%	95.9%
		Negative	Count	0	3	3
			%	0.0%	4.8%	4.1%
	Total		Count	12	62	74
			%	100.0%	100.0%	100.0%
CSF:Sensitivity=100%Specificity=4.8 %Positive predictive value=16.9% Negative predictive value= 100%Accuracy rate=20.3%						

Table 5: Leukocyte analysis of all body fluids

			Positive	Negative	Total
Leukocyte	Positive	Count	17	0	17
		%	35.4%	0.0%	9.0%
	Negative	Count	31	141	172
		%	64.6%	100.0%	91.0%
Total		Count	48	141	189
		%	100.0%	100.0%	100.0%
a. X2=54.873p<0.001 vhs					
b. Sensitivity= 35.4 %Specificity=100.0%Positive predictive value=100%Negative predictivevalue=81.9%Accuracy rate= 83.6%					

Table 6: Protein analysis of all body fluids

			Positive	Negative	Total
Protein	Positive	Count	55	7	62
		%	72.4%	6.2%	32.8%
	Negative	Count	21	106	127
		%	27.6%	93.8%	67.2%
Total		Count	76	113	189
		%	100.0%	100.0%	100.0%
a. x2=90.267p<0.001 vhs					
b. Sensitivity= 72.4 %Specificity=93.8%Positive predictive value=88.7%Negative predictivevalue=83.5%Accuracy rate= 85.2%					

Table 7: Comparison of Present Study with Similar Previous Studies

Fluid	Study	Parameter	Sensitivity	Specificity	PPV	NPV	Accuracy
	Present study	Leukocyte	36.4%	100%	100%	90%	90.5%
		Protein	36.4%	100%	100%	90%	90.5%
		Glucose	100%	4.8%	16.9%	100%	20.3%
	MR Manjunath et al,[8] (2022) 30 samples	Leukocyte	78.6%	68.6%	68.6%	78.6%	86.7%
		Protein	41.7%	88.9%	71.4%	69.6%	93.3%
		Glucose	50%	92.3%	50%	92.3%	83.3%
	Noman O et al,[9] (2021) 100	Leukocyte	95.9%	96.2%			96%

ISSN (O): 2687-5365; ISSN (P): 2753-6556

CSF	samples	Protein	97.3%	96.1%			97%
		Glucose	91.2%	65.3%			85%
	Ganesh R et al,[10] (2020) 100 samples	Leukocyte	92%	98.7%	95.8%	97.4%	97%
		Protein	93.8%	98.8%	93.8%	98.8%	98%
		Glucose	50%	100%	100%	86.4%	88%
	Wankhade R et al,[1] (2020) 50 samples	Leukocyte	82.4%	100%	100%	47.1%	84.8%
		Protein	78.6%	100%	100%	33.3%	80.7%
		Glucose	100%	78.9%	92%	100%	93.9%
	Gupta A et al,[11] (2019) 360 samples	Leukocyte	100%	96%			92%
		Protein (1+)	99%	54%			89%
		Glucose	98%	92%			100%
	Mazumder S et al,[12] (2018) 100 samples	Leukocyte	89.3%	98.6%	96.6%	95.9%	96%
		Protein	95.8%	98.7%	95.8%	98.7%	98%
		Glucose	48.2%	100%	100%	82.6%	85%
	Chikkannaiah P et al,[13] (2016) 103 samples	Leukocyte	96.6%	94.5%	87.8%	98.5%	
		Protein	96%	87.1%	70.5%	98.5%	
		Glucose	14.2%	100%	100%	75.7%	
	Joshi et al,[2] (2013) 75 samples	Leukocyte	85.2%	89.6%	82.1%	91.5%	
		Protein	92.6%	87.5%	80.6%	95.5%	
		Glucose	46.2%	98%	92.3%	77.4%	
Pleural	Present study	Leukocyte	28.6%	100%	100%	57.4%	63.6%
		Protein	85.4%	92.9%	97.2%	68.4%	87.3%
	Kalaisezhian N et al,[14] (2018) 84 samples	Leukocyte	90.2%	66.7%	97.3%	33.3%	88.6%
	Azoulay E et al,[15] (2000) 82 samples	Leukocyte	42.8%	91.3%	88.2%	51.2%	
		Protein	93.1%	50%	84.3%	71.5%	
Ascitic	Present study	Leukocyte	50%	100%	100%	92.3%	92.8%
		Protein	65%	83.3%	68.4%	81.1%	76.8%
	Khairnar H et al,[16] (2020) 64 samples	Leukocyte	100%	94%	57%	94%	94.5%
	Ashish Jha et al,[17] (2012) 100 samples	Leukocyte	77.8%	95.1%	77.8%	95.1%	92%
	Sapey et al,[18] (2005) 184 samples	Leukocyte	64.7%	99.6%	91.7%	97.4%	
	Kim et al,[19] (2005) 75 samples	Leukocyte	50%	100%	100%	87%	
	Butani et al,[20] (2004) 90 samples	Leukocyte	89%	99%	89%	99%	

DISCUSSION

The diagnostic accuracy rate was 90.5% for detection of CSF granulocytes of >15 cells/mm^3. The leukocyte esterase cut-off was grade 2 to distinguish infectious exudates from non-infectious exudative effusions and the diagnostic accuracy rate was 63.6% and 92.8% for pleural and ascitic fluid respectively.

The urine reagent strips showed 7 false negative leukocyte count in CSF samples, 20 in pleural fluid and 4 in ascitic fluid samples. These samples had lymphocytic leukocytosis on differential leukocyte count by Neubauer chamber method. The likely reason for false negatives was that the leukocyte esterase test is specific for granulocytes and could not detect other white blood cells. Hence we need to design a better pan‐leukocyte marker, which will be more accurate.

The normal count of leukocytes in CSF is 0–7 cells/mm^3 and the reagent strip method fails to give exact count of leukocytes which is important for the diagnosis of meningitis as the sensitivity of reagent strip test is >15 cells/mm^3 and chances of missing the diagnosis in cases of cell count between 7-15 cells/ mm^3.

The protein level cut-off in CSF was grade 2 and to distinguish transudates from exudative effusions was 300mg/dl corresponding to grade 3 in the reagent strip. The diagnostic accuracy rate for detection of proteins in CSF, pleural and ascitic fluid were 90.5%, 87.3% and 76.8% respectively.

The index test showed one false positive case in pleural fluid and 6 cases in ascitic fluid. The reason could be presence of RBCs in the fluid sample.

The definitive test showed protein values of >100 mg/dl (more than 2+) in 11 cases whereas the index test showed CSF proteins >100 mg/dl in only 4 cases. There were 7 false negative cases in CSF, 6 in pleural fluid and 7 in ascitic fluid samples.

Protein level is required to categorize the type of meningitis. Main problem lies in distinguishing between a 2+ CSF protein as normal or abnormal. A simple solution to this problem can be repeat testing of a 2+ CSF in double dilution. By this method, protein levels between 45 and 100 mg/dl can be identified.

The false-negative diagnosis appears to be a drawback of reagent strip method as it has cutoff, and therefore, the value lower than cut-off which is detected by definitive test is recorded negative by reagent strip method, resulting in erroneous interpretation of fluid examination.

The diagnostic accuracy rate for detection of CSF glucose level was 20.3%. The index test showed very low specificity and low diagnostic accuracy

ISSN (O): 2687-5365; ISSN (P): 2753-6556

because of high false positive cases. The reason for false positives was that the reagent strip color grading had the least value of <100mg/dl indicating no color change. So there was difficulty in differentiating between normal CSF samples from abnormal samples. Use of urine reagent strips from different manufacturers would have increased the diagnostic accuracy rate as the least value for detection of glucose would have been <50mg/dl.

The diagnostic accuracy of CSF leukocyte and protein in the present study was almost similar to other studies. Whereas, other studies had good specificity and diagnostic accuracy of glucose in CSF compared to the present study. A study by Kalaisezhian N et al had a good diagnostic accuracy of pleural fluid leukocyte value compared to the present study and a study by Azoulay E et al, because Kalaisezhian N et al calculated the results for only infectious pleural effusion other than tuberculosis.

There was statistical comparison of ascitic fluid leukocyte count in the present study with other studies. Majority of the studies on ascitic fluid and pleural fluid showed comparison of only leukocyte esterase reagent strips with the laboratory values and there were no studies to compare the accuracy of protein values. [Table 7].

The likely reason for false negatives and positives could be due to variations in the normal cut-off values in body fluid samples as compared to urine. We can overcome this problem by designing reagent strips at the manufacturer's level that are specific for individual body fluids and include only three parameters i.e, protein, glucose and granulocyte, thereby making the fluid analysis more cost effective.

The leukocyte and protein positivity by strip test in all 3 body fluid samples were statistically significant and had the diagnostic accuracy rate of 83.6% and 85.2% respectively. There is no single study to compare the utility of urine reagent strips in all 3 body fluid samples.

Limitation: Majority of the CSF samples had normal study and hence there was difficulty in assessing the efficacy of urine reagent strips to diagnose meningitis. As synovial samples were very less in number, we could not analyse the diagnostic utility of reagent strips to classify synovial fluid as non-inflammatory or inflammatory.

CONCLUSION

The results of our study and with reference to the results obtained in similar studies by various observers, we can demonstrate that urine reagent strips can reliably predict raised CSF protein (>100 mg/dl) and increased granulocyte count (>15 cells/mm^3). It can also differentiate transudates from exudative effusions and infectious exudates from non-infectious exudative effusions in pleural and ascitic fluids. The reagent strip could be a feasible option and a promising diagnostic tool for a faster and cheaper diagnosis of SBP. Hence, the reagent strip test is a rapid, easy-to-use, inexpensive tool and can be of value to clinicians working in resource‑limited settings by prompting early diagnosis of meningitis and SBP so that appropriate treatment can be initiated and can save lives from these lifethreatening conditions.

REFERENCES

1. Wankhade R, Bhake A. Assessment of efficacy of urinereagentstrips for cerebrospinal fluid analysis as emergency workup in critical care setup. J Datta Meghe Inst Med Sci Univ2020;15:526-32.
2. 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; 4:140-5.
3. Light RW. Diagnostic principles in pleural disease. Eur Respir J 1997;10: 476–81.
4. Light RW, Mac Gregor I, Luchsinger PC,et al.Pleuraleffusion: thediagnostic separation of transudates and exudates. AnnInternMed1972; 77:507–13.
5. Rimola A, Garcia-Tsao G, Navasa M, et al. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document. J Hepatol 2000; 32:142-53.
6. Garcia-Tsao G, Conn H.O, Lerner E. The diagnosis of bacterial peritonitis: comparison of pH, lactate concentration and leukocyte count. Hepatology 1985; 5:91-6.
7. P Ravaud, C Hudry, B Giraudeau, B Weill, M Dougados. Rapid diagnosis of inflammatory synovial fluid with reagent strips. Rheumatology 2002; 41:815-8.
8. Manjunath MR, Tasneem R, Malathi BG, Srujan HP. Utility of urine reagent strips for analysis of cerebrospinal fluid in emergency settings: A cross-sectional study. J of clinical and diagnostic research 2022; 16(5):46-9.
9. Noman O, Bhatt N, Dawande P, Chaudhary GA. Assessment of utility of urine reagent strips for analysis of cerebrospinal fluid (CSF) in emergency settings for rapid clinical interventions.Nat.Volatiles&Essent.Oils 2021; 8(5): 1148-53.
10. Ganesh RA, Prabhu MH. Utility of urine reagent strips in CSF analysis as an aid to rapid diagnosis of meningitis. Annals of Pathology and Laboratory Medicine 2020; 7(6): 306-10.
11. Gupta A, Dwivedi T. Reagent strips test: A simplified method for prompt analysis of cerebrospinal fluid in neurological disorders in emergency. Practical Laboratory Medicine.2019;16:e00124.
12. Mazumder S, Ramya B S, Biligi DS. Utility of urine reagent strips in cerebrospinal fluid analysis: An aid to bedside diagnosis of meningitis. Indian J PatholMicrobiol2018;61:356-9.
13. 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;64:50-5.
14. Kalaisezhian N, Irsath S, Shankar R. Validity of leukocyte esterase reagent (LER) strip in diagnosing infectious pleural effusion. Int J Adv Med 2018;5:1041-6.
15. Elie Azoulay, Fartoukh M, Galliot R, Baud F, Simonneau G,Roger J, et al. Rapid Diagnosis of Infectious Pleural Effusions by Use of Reagent Strips: Clinical Infectious Diseases 2000;31:914–9.
16. Khairnar H, Ingle M, Pandey V, Kolhe K, Chauhan S, Sawant P, et al. Accuracy of Leukocyte Esterase Reagent Strip (LERS) test for rapid bedside screening of spontaneous bacterial peritonitis: An observational study. J Family Med Prim Care 2020;9:5542-6.
17. Jha AK, Kumawat DC, Bolya YK, Goenka MK. Multistix 10 SG leukocyte esterase dipstick testing in rapid bedside diagnosis of spontaneous bacterial peritonitis: A prospective study. J Clin Exp Hepatol 2012;2:224‑8.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

18. Sapey T., Kabissa D., Fort E., et al. Instant diagnosis of spontaneous bacterial peritonitis using leukocyte esterase reagent strips: Nephur-Test vs. Multistix SG. Liver Int 2005;25: 343-8.
19. Kim do Y., Kim J.H., Chon C.Y., et al. Usefulness of urine strip test in the rapid diagnosis of spontaneous bacterial peritonitis. Liver Int 2005;25:1197-201.
20. Butani RC, Shaffer RT, Szyjkowski RD, Weeks BE, Speights LG, Kadakia SC. Rapid diagnosis of infected ascitic fluid using leukocyte esterase dipsticktesting. Am J Gastroenterol. 2004;99:532–7.

ISSN (O): 2687-5365; ISSN (P): 2753-6556