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Role of urine reagent strips in cerebrospinal fluid analysis – An aid to bedside diagnosis of meningitis in the paediatric age group

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***Abstract**:*
***Context**: The examination of the cerebrospinal fluid (CSF) for proteins, glucose, and leukocytes remains the basic gold standard investigation for the initial diagnosis of meningitis. Early diagnosis and initiation of antibiotics within 3 hr can reduce the mortality and morbidity associated with meningitis. Hence, we conducted this study to document the usefulness of urinary reagent strip for the semi-quantitative analysis of CSF chemistry and cellularity as an aid to bedside diagnosis at a tertiary care centre for paediatric age group.*
***Aim**:We conducted this study,1) To evaluate and establish the role of urine reagent strip for rapid diagnosis of meningitis in CSF analysis in paediatric age group2) To facilitate the early therapeutic decisions and to rule out the diagnostic dilemma for the clinicians.*
***Material and method**:100 samples of CSF were received in the laboratory of a tertiary care hospital, Ahmedabad. All CSF samples were subjected to two types of tests-the definitive test and the index test. CSF microscopy for leucocytes as well as biochemistry tests for protein and glucose on automated biochemistry analyser were considered as a definitive test. The index test for protein, glucose, leucocyte for the same sample was conducted by urinary reagent strip.*
***Result**:The strip test showed a sensitivity of 97.29% and a specificity of 92.06% for proteins. With respect to glucose, the strip was sensitive 65.21%as well as highly specific 100%.It showed high sensitivity and specificity for leukocytes ≥ 15 cells/cummi.e., 94.11% and 98.79% respectively. The accuracy of this three parameters tests- leucocytes, proteins, glucose are 98%,94%,92% respectively.*
***Conclusion**:The Urinary reagent strip can be used routinely at the bedside for rapid analysis of CSF especially for meningitis. If implemented, this technique will be useful especially in emergency settings as well as in areas with limited resources.*
***Key Words**:Urine reagent strip, Cerebrospinal fluid, Meningitis.*

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I. Introduction

Meningitis is a severe, life-threatening infection of the central nervous system that requires immediate medical attention and delaying its diagnosis, treatment can cause permanent neurological deficits and death. For its diagnosis, analysis of cerebrospinal fluid is performed in an emergency. In the paediatric age group, meningitis is a common disease responsible for morbidity and mortality.CSF examination is not available in the small set-ups with limited resources. So, the CSF samples from these areas are sending to the higher laboratory which results in the delay of diagnosis and start of the initial treatment. In such cases, the urinary reagent strip method can be used to assess CSF. These urinary reagent strips provide a semi-quantitative estimation of CSF chemistry and cellularity.

It is simple to use, rapid, low cost and do not require any expertise. The present study was conducted to decide the role of urinary reagent strip for CSF analysis at the bedside for rapid diagnosis of meningitis like emergency conditions in paediatric age group at tertiary care centre..

II. Subject And Method

We conducted a single-blinded prospective study of 100 CSF samples received in our laboratory within an hour of a tap. Traumatic(bloody CSF) taps were excluded from our study. After performing a gross examination of CSF for appearance and colour (normal is colourless and clear), both definitive test and the index test were carried out as described below for all the samples received from the paediatric ward.

Index test:The index test was done by using urinary reagent strip which can detect ten parameters including protein, sugar, leukocyte esterase. Undiluted CSF was mixed with the micropipette and 2–3 drops of CSF was then added to patches of leucocytes, proteins, sugar and reaction were noted after 30–60 s. Then, reaction colours of the test area were compared with the colour chart on the label.

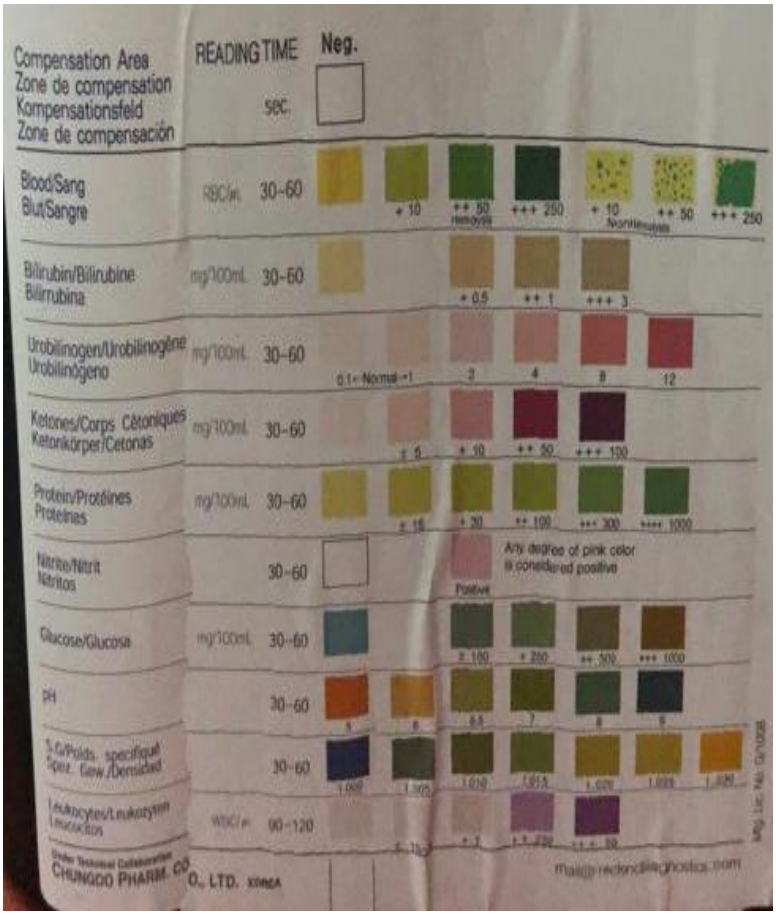

Figure 1. Colour chart of urine reagent strip used in present study

- The strip can detect the leucocytes from 15 to 500 cells/mm³. It can detect the leucocytes by estimation of leucocyte esterase. Leucocytes are grades as negative for cell count of < 15 cells/mm³ , traces for 15-25 cells/mm³, 1+ for 25-75 cells/mm³, 2+ for 75-250 cells/mm³ and 3+ for 250-500 cells/mm³.
- For protein, gradings are <15 (mg/dl) is negative(normal). 1+ for 15- 30 (mg/dl), 2+ for 30-100(mg/dl), 3+ for 100-300 (mg/dl), 4+ for 300-1000(mg/dl).
- For sugar, no colour change for <50 mg/dl. Traces for 50-100 mg/dl. 1+ for 100-250 mg/dl,2+ for 250-500 mg/dl, 3+ for 500-1000 mg/dl.

Definitive test:Total cell count for leucocytes were done manually from undiluted CSF sample on modified Neubauer chamber immediately after receiving the sample.Other reference standard tests like CSF protein and glucose were performed in the biochemistry analyser.

Statistical analysis: Statistical analysis was performed to compare the accuracy of the reagent strip versus the standard tests using the specificity, sensitivity, positive predictive value, negative predictive value. We also constructed receiver operating curves (ROC) to evaluate the overall performance of index tests and estimated area under the curve (AUC) along with standard error (SE).

III. Results

This study was conducted on 100 consecutive CSF samples of paediatric patients. There were 55 males and 45 females(ratio was1:1).Neonates are most effective here.

Table 1. Age-wise distribution of cases

Age	Male	Female	Total
0-1 month	28	14	42
2 months-1 year	12	15	27

2 years-5 years	08	10	18
6 years – 10 years	03	04	07
11 years-15 years	04	02	06
Total	**55**	**45**	**100**

- Three main parameters – leucocytes, proteins and glucose of both tests for all samples were compared with reference standards.
- The strip test showed a sensitivity of 97.29% and a specificity of 92.06% for proteins levels >30mg/dl. The sensitivity and specificity increased with higher cut-offs of protein level.
- With respect to glucose, the strip was highly specific 100% and less sensitivity 65.21%.It showed high sensitivity and specificity for leukocytes ≥ 15 cells/cumm i.e., 94.11% and 98.79% respectively.

Table2.Result of present study - leucocyte count,protein,sugar

Parameter	Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)	Accuracy(%)
Leucocytecount	94.11	98.79	94.11	98.79	98
Protein	97.29	92.06	84.80	98.30	94
Sugar	65.21	100	100	90.58	92

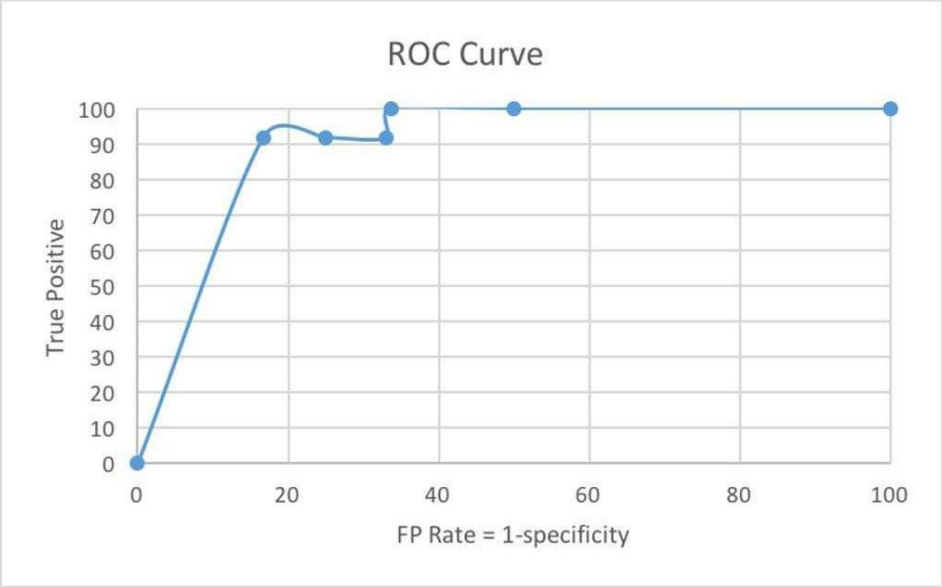

Figure 2. Receiver operating curve for leucocyte count

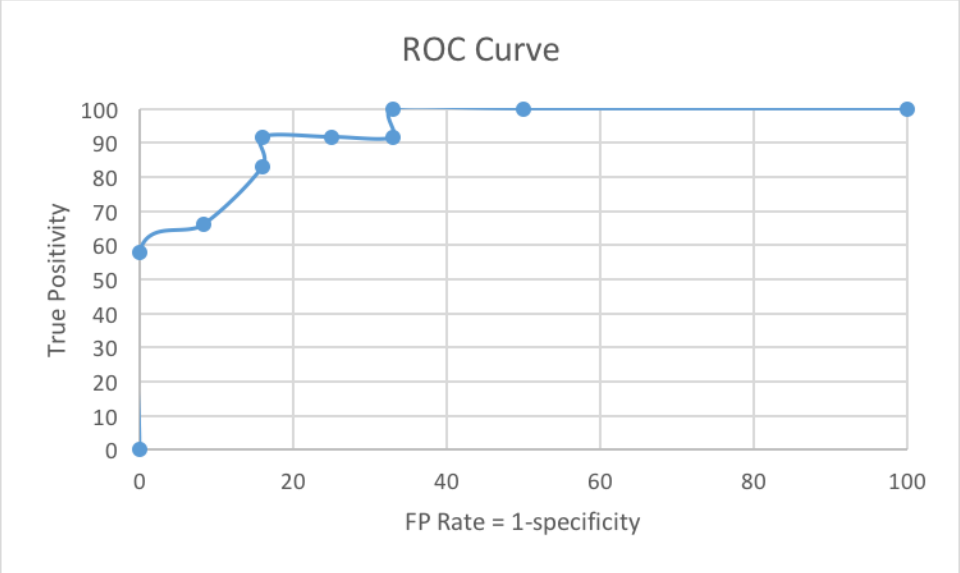

Figure 3. Receiver operating curve for proteins

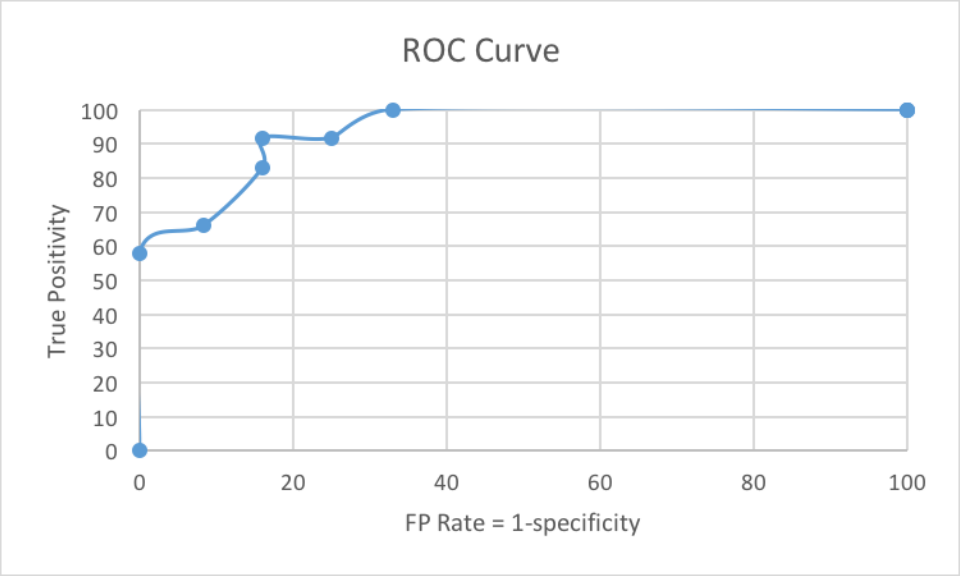

Figure 4. Receiver operating curve for sugar

Table 3. Comparison table between present study results and the literature review

	Present study	**Chikkannaiah et. al., (2016)**	**Joshi et al., (2013)**	**Parmar et al., (2004)**
No. of cases	100	103	75	63
Leucocytes >15 cells/cumm	Sensitivity-94.11% Specificity-98.79% AUC-97.96%	Sensitivity-97% Specificity-94% AUC-99%	Sensitivity-85% Specificity-89% AUC-87%	Sensitivity-97% Specificity-96%
CSF protein	Sensitivity-97.29% Specificity-92.06% AUC-95.32%	Sensitivity-95% Specificity -46% AUC-85%	Sensitivity-98% Specificity-57% AUC-77%	Not done
CSF glucose	Sensitivity-65.21% Specificity-100% AUC-90.03%	Sensitivity-29% Specificity -100% AUC-78%	Sensitivity-61% Specificity-97% AUC-78%	Not done
Spectrum of Cases	Most cases are meningitis	-	-	-

(AUC=Area under curve)

IV. Discussion

Observations of present study were similar to some previous studies conducted especially in meningitis. Chikkannaiahet al. (2016) have used urinary strips for semi-quantitative analysis of CSF cellularity and chemistry and have observed high sensitivity and specificity in leucocytes estimation. Parmar et al. (2004) reported the sensitivity and specificity of the reagent strips for the diagnosis of meningitis as 97.14% and 96.42%, respectively and accuracy observed for diagnosis of meningitis. Joshi et al(2013). observed a more specificity(97%) for glucose than other parameters.

Limitations of our study is less number of samples, mostly paediatric age group patients and despite of colour grading matching very carefully, findings were subjective. Reagent strips can be stored at 2-30˚C and in a tightly capped container.

V. Vi. Conclusion

- In present study, urine reagent strips were most sensitive for proteins and more specific for sugar. We additionally observed that accuracy of test increased with increasing the value of leucocyte count and protein, sugar. The accuracy of this three parameters tests- leucocytes, proteins, glucose are 98%,94%,92% respectively.This tests also show high leucocyte count and protein levels and low sugar level which is relevant for meningitis
- From present study, we can conclude that urinary strips can be used for cerebrospinal examination in case of meningitis mainly to facilitate therapeutic decisions.

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