

Correspondence

Comment on: Sensitivity and specificity of cerebrospinal fluid glucose measurement by an amperometric glucometer

To the Editor

I read with interest the article written by Alkhalifah et al.¹ Rapid diagnosis of meningitis and early treatment improves the outcome and decreases the associated complications. Quickly measured cerebrospinal fluid (CSF) and serum glucose, and their ratio, along with other indices, helped in timely treatment decisions.² The gold standard for glucose measurement is a laboratory-based technique which is laborious and time-consuming.² Alternatively, point of care glucose measurement using a glucometer is easy to use and quick.

The current study explored a crucial diagnostic technique that may assist clinicians in treatment decisions related to a life-threatening emergency.

The authors aimed to test the accuracy of amperometric glucometer (AG) in measuring cerebrospinal fluid (CSF) glucose and compare it with the conventional laboratory technique (CLT).

The authors found 47 samples had hypoglycorrhachia identified by CLT, and the AG detected 17% of them. Similarly, CLT showed 54 cases with normal CSF glucose; 53 were recognized as normal by AG.

There are many unanswered questions in the methodology adopted by the authors, the statistical analysis, the interpretation of findings, and the potential application of their results.

The authors stated that the study duration was 15 months (March 2017 to September 2018). However, this period is 18 months. This may need clarification.

Patients were classified into normal CSF group or high clinical suspicion of meningitis group according to the culture, CSF glucose, protein, and cells. However, no clear definition of 'high clinical suspicion of meningitis' was cited. One wonders would a patient with a combination of some normal and abnormal parameters considered to have 'high clinical suspicion of meningitis' or not.

The method adopted by the authors entail measuring CSF glucose by CLT and AG; however, serum glucose was measured by CLT only. As the CSF/serum glucose ratio is an essential parameter in clinical decision making, it would be appropriate to have both indices measured by the same method.³ Furthermore,

measuring both CSF and serum glucose by AG will enable the physician to calculate the ratio at the point of care and hence aid in the therapeutic intervention.

Samples with CSF laboratory analysis taking more than one hour were excluded. It would be more informative to observe and compare the turnaround time for both CLT and AG. This gives the reader an objective measure of how quickly the method is used for analysis reflected in the timely management of patients.

The authors based their statistical analysis on showing the correlation between the CSF glucose obtained by CLT and AG. It would be helpful to perform additional clinically oriented statistical analysis to inform physicians on the performance of the 2 tests regarding diagnostic decision making. For example, one would like to know how many samples had proven bacterial meningitis (culture and positive gram stain) the glucometer failed to identify and compare this with CLT. It is imperative to state clearly how many CSF hypoglycorrhachia missed by AG in the 'high clinical suspicion of meningitis' group compared to CLT and the statistical significance of the difference. Also, one would like to know how many samples reported by CLT as normal and detected by AG as hypoglycorrhachia. Furthermore, logistic regression analysis helps to understand the relationship between culture-proven bacterial meningitis with independent variables like CSF/serum glucose using both techniques.

The CSF/serum glucose ratio is an essential tool in diagnosing meningitis in the point of care setting. However, the authors did not report any data regarding this parameter.³

Alkhalifah et al¹ concluded that AG was 89% sensitive and only 42.3% specific in all samples analyzed. With this low specificity, I would be reluctant to recommend AG in the point of care setting to measure CSF glucose. The authors are expected to discuss the implications of their results on clinical decision-making and highlight the pros and cons of adopting AG based on their findings.

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Reply from the Author

We have received the correspondence written by Prof. Sarar Mohamed, and we are glad that our study titled, "Sensitivity and specificity of cerebrospinal fluid glucose measurement by an amperometric glucometer"

caught his interest.¹ We have taken his comments and observation into consideration.

Regarding the study duration, it was as written from March 2017 to September 2018 (18 months in total). What was written in the original manuscript that the study took 15 months duration was a overlook.

The patients included in our study were classified into the normal CSF group indicating that they had normal glucose, protein, white blood cell (WBC) counts, and cultures, while the group of high clinical suspicion of meningitis included any patient who had any abnormal CSF parameters as mentioned in the study methods in the published manuscript. Patients having negative CSF culture with other abnormal CSF parameters and clinical presentation suggestive of meningitis were included in the high clinical suspicion of meningitis group.

Regarding serum glucose measurements, it was carried out using the same point of care AG used for the CSF glucose measurement within one hour before CSF sampling as mentioned in the manuscript. We did not include serum glucose measurement by standard laboratory techniques in our study methodology as blood extraction for patients present with clinical suspicion of meningitis was carried out early before CSF sampling in our institution, which makes time gap between the samples longer. We aimed to use serum glucose measurements just before doing the CSF sampling for better accuracy to avoid any other confounding factors that might influence the glucose measurements like delay in laboratory analysis.

Our study, as mentioned, excluded all the CSF samples that took more than one hour to be analyzed. We did not study the difference between CSF samples done earlier and later as it was studied and described previously by Rajesh et al⁴ and Mlinarić et al.⁵

Further statistical analysis to answer the questions raised by Prof. Sarar showed that 4 patients had positive bacterial CSF cultures. Approximately 25% of them found to have hypoglycorrhachia, while 50% found to have CSF to serum glucose ratio of <0.6 using both standard laboratory analysis and POC AG. Samples identified to have hypoglycorrhachia by both methods within the groups included in the study described in [Table 1](#), and a comparison between the 2 methods used in detecting hypoglycorrhachia described in [Table 2](#). Similarly, a detailed analysis for CSF/Serum ratio described in [Table 3](#).

From [Table 3](#), we can observe that AG sensitivity and specificity in detecting CSF/serum ratio <0.6 were 89% and 42.3%, compared with the standard laboratory analysis sensitivity of 100% and specificity of 74%. Unlike previous studies which demonstrated a better

Table 1 - Hypoglycorrhachia frequency per clinical suspicion of meningitis.

Samples	Standard laboratory analysis		Amperometric glucometer	
	Hypoglycorrhachia	Normal glucose	Hypoglycorrhachia	Normal glucose
Highly suspicious	4	57	3	58
Normal CSF	0	40	0	40

CSF: cerebrospinal fluid

Table 2 - Comparing standard laboratory analysis with amperometric glucometer in detecting hypoglycorrhachia.

Standard laboratory analysis	Amperometric glucometer	
	Hypoglycorrhachia	Normal glucose
Hypoglycorrhachia	3	1
Normal glucose	0	97

Table 3 - Cerebrospinal fluid/serum ratio <0.6 frequency per clinical suspicion of meningitis.

Samples	Standard laboratory analysis		Amperometric glucometer	
	CSF/serum ratio <0.6	Normal CSF/serum ratio	CSF/serum ratio <0.6	Normal CSF/serum ratio
Highly suspicious	47	14	8	53
Normal CSF	0	40	1	39

specificity compared to this study, we used different POC device, which uses different analysis technology.^{6,7} We also had larger sample size and included both neonates and children age groups.

Overall, the results of this study suggesting that AG can be used as a potential tool for measuring CSF glucose to strengthen the clinical suspicion of meningitis along with the clinical presentation, which can influence earlier antibiotics administration. This tool might be helpful when standard laboratory analysis is not feasible though further studies are needed. One of the disadvantages of such a tool is that there are multiple brands and techniques used for measuring glucose levels, which can influence the accuracy of the results. This study only included one glucometer device that used amperometry technique for measuring glucose level.

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