Original Article

ACCURACY EVALUATION AND COMPARISON OF THREE BLOOD GLUCOSE METERS IN AN EMERGENCY PAEDIATRIC UNIT OF A TERTIARY HOSPITAL IN NIGERIA.

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ABSTRACT

BACKGROUND
Advances in technology have made available different types of glucose meters for use at the patient's bed side with significant variation in accuracy among these glucose meters.
OBJECTIVES
We evaluated the accuracy of three commonly used glucose meters in a children emergency room using laboratory method as reference.
SUBJECTS
Subjects were 206 children seen in emergency room over a period of 3 months.
METHODS
Capillary blood glucose was determined at the bed side using three glucose meters: Accu - Chek® Active, On Call® Plus and One Touch® Ultra Mini. Peripheral venous blood was simultaneously collected for comparative plasma glucose analysis at the laboratory.
The mean absolute relative deviations (MARDs) were determined. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated.
RESULTS
The MARD for Accu - Chek® Active, On Call® Plus and One Touch® Ultra Mini were 11.58%, 27.00%, and 13.91% respectively. In the diagnosis of hyperglycaemia, the sensitivity and specificity for Accu - Chek® Active, On Call® Plus, One Touch® Ultra Mini were 83.3% and 96.3%, 94.4% and 79.3%, 94.4 and 94.7% respectively. The PPV and NPV for Accu - Chek® Active, On Call® Plus, One Touch® Ultra Mini were 68.1% and 98.4%, 30.4% and 99.3%, 62.9% and 99.4% respectively. Four cases of hypoglycaemia were detected by the laboratory method and the 3 glucose meters detected 3 out of the 4 correctly.
CONCLUSION
These three glucose meters varied in accuracy but the glucose values by the Accu - Chek® Active had the least variation from the laboratory results.
KEY WORDS: Glucose meter, hyperglycaemia, hypoglycaemia, Dysglycaemia, Emergency Paediatric Unit.

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INTRODUCTION

Glucose meter is a point-of-care (POC) instrument that is commonly used to rapidly measure blood glucose and it is cheaper to use especially when there is need for serial blood glucose monitoring. Low sample volume plus rapid results allow for frequent serial measurements which in turn allow for more aggressive management of dysglycaemia in an emergency setting.
Dysglycaemia complicating acute illnesses are common findings in children emergency room and this has been associated with increased morbidity and mortality.There is an increasing evidence that maintaining as close to normal glucose as possible in hospitalized patients can significantly improve outcomes, reducing both morbidity and mortality. Hence achieving target glycaemic levels using accurate blood glucose monitoring device is necessary to improve outcomes of hospitalized patients.
Recent advances in technology have made available different types of glucose meters, utilizing various methodologies with significant variation in accuracy among these glucose meters. Although, most existing blood glucose meters were submitted for approval by regulating bodies like the United States Food and Drug Administration (FDA) however, evaluation studies needed for their approval were conducted majorly on clinically stable outpatient adults with diabetes. But sick children presenting in emergency room have a wide range of medical problems (such as hypotension, shock, severe dehydration, and anaemia,) complicating their primary illness and these may affect glucose meter accuracy.Other physical factors like altitude, humidity and temperature can also influence the accuracy of blood glucose strips.It may therefore be necessary for glucose meters to be evaluated before use, and the specific meter model selected should be based on its performance in the intended patient population and environment.

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The accuracy of glucose meters is usually assessed by comparison to a method in routine use in the clinical laboratory.It is important to know by how much a glucose meter is likely to differ from the routine laboratory results. It is also equally necessary to determine the precision (the reproducibility of a series of values), independent of the closeness of any of the values to the reference. Only when a series of values is both accurate and precise do the individual values actually reflect the reference value. One of the simple and very reliable measure of both accuracy and precision is the mean absolute relative deviation (MARD) and this is calculated by taking the average for the set of individual absolute errors relative to its reference value.Lower MARD value indicates smaller difference between a glucose meter value and the reference value and a higher MARD value indicates larger difference between meter value and the reference value.

Glucose meters are used to confirm or refute the presence of hypo or hyperglycaemia or for monitoring blood glucose level in children's emergency room. The accuracy of a glucose meter in diagnosing or excluding these conditions when present or absent in the patients can be determined using predictive indices (sensitivity, specificity, positive and negative predictive values).The sensitivity of a clinical test refers to the ability of the test to correctly identify those patients with the disease. A high sensitivity is clearly important where the test is used to identify a serious but treatable disease. The specificity of a clinical test refers to the ability of the test to correctly identify those patients without the disease. A test with a high sensitivity but low specificity results in many patients who are disease free being told of the possibility that they have the disease and are then subjected to further investigation or wrong treatment. Positive predictive value (PPV) of a test is the probability that this patient has the disease given that the test result is positive. Negative predictive value (NPV) of a test is the probability that this patient does not have the disease given that the test result is negative.

Evaluation and direct comparison of many available glucose meters in the children emergency setting is scarce. The few published studies evaluated a single glucose meter or evaluated performance in detecting hypoglycaemia and did not test across the full range of glucose levels.Glucose meter may not be very accurate across the full range of glucose values and more importantly cases of hyperglycaemia are also encountered in the paediatric emergency room. It is most unlikely that different glucose meters will agree exactly, by giving the identical result for all individuals.This study evaluated and compared the accuracy of three commonly used glucose meters: Accu - Chek® Active (Roche diagnostics, Mannhiem, Germany), On Call® Plus (Acon Lab. Inc San Diego, USA), and One Touch® Ultra Mini (Life Scan, Switzerland).

It compared the blood glucose values of the three glucose meters against the glucose values reported from our hospital central laboratory method in order to know by how much a glucose meter is likely to differ from the laboratory results. If this is not significant enough to cause problems in clinical interpretation one can replace the laboratory by the glucose meters or use the two interchangeably. We also compared the performance of the glucose meters in the bedside diagnosis of hypo and hyperglycaemia using sensitivity, specificity and predictive values

METHODS

This study was conducted in the Emergency Paediatric Unit (EPU), Department of Paediatrics of Ahmadu Bello University Teaching Hospital (ABUTH), Shika-Zaria. The study was a cross-sectional prospective study.

A total of 206 patients aged 1 month -13 years seen in EPU, whose parents/care givers consented to participate in the study, were serially recruited. Patients whose venous sampling could not be done were exempted from the study. The study was done from October 2015 to January 2016.

Approval for the study was obtained from the Health Research Ethics Committee (HREC) of ABUTH before commencement of the study. Informed written consent was obtained from parent(s) or care-giver(s) of the subject before enrolment into the study. Assent was obtained from children aged 8 years and above. Results of patients with abnormal glucose levels were communicated immediately to their primary physician for appropriate management and monitoring.

Data collection

A semi structured questionnaire designed for the study was used to obtain relevant information about the patient including the bio-data, presenting complaints and anthropometric measurement.

Sample collection and preparation

Capillary blood was taken with three different glucose meters (Accu - Chek® Active, On Call® Plus and One Touch® Ultra Mini) and glucose values obtained were recorded. The determination of glucose meter sequence was randomly assigned. The areaof measurement was disinfected with methylated spirit before pricking and the first drop of blood removed with a sterile dried swab. All the measurements were carried out with one single subsequentdrop from the same site. Commercial test strips with identical lots number were used for the study. The test strips were stored in the original container. Strips were used immediately after removal from the vial and the test strips container closed immediately after taking a test strip. All measurements were performed in line with the instructions provided in the manual booklets.

A venous blood sample was collected from a convenient peripheral vein in the upper limb within five minutes of the finger prick tests.About 2 mls of peripheral venous blood was taken from the subject and dispensed into fluoride-oxalate containing tube. The site to be used for bloodletting was cleaned with methylated spirit using a sterile swab.

The fluoride-oxalate containing sample was separated, within one hour after collection, at the side laboratory and the plasma sent to the central laboratory for glucose analysis. The plasma glucose was measured by spectrophotometer (mrc SPECTRO V-16) using glucose oxidase test kit (Glucose, Agappe diagnostics SwitzelandGmbH) and the glucose values documented. The glucose determination was done according to the method described by Trinder.() Hyperglycaemia and hypoglycaemia were defined as blood glucose greater than 140mg/dl (7.7mmo/l), and less than 45mg/dl (2.5mmol/l)

respectively.
The packed cell volume (PCV) of all the subjects was determined using a micro haematocrit method using a portion of the oxalated blood.() Two thirds of the capillary tube was filled with the oxalated venous blood and the other end sealed with plasticine. The tube was centrifuged for five minutes using a micro haematocrit centrifuge. A Haematocrit value was read manually with a micro haematocrit reader.

Stastistical analysis
Statistical analysis was performed using the statistical software SPSS version 20 and GraphPad Instat (GraphPad Software. Inc.). Measures of variations (Mean errors. standard deviations, coefficient of variation) were determined. The MARD was calculated as, absolute value of the difference between glucose meter readings and reference divided by the reference, expressed as percentage. Using the blood glucose from the laboratory as the reference, the sensitivity, specificity, positive and negative predictive values of blood glucose obtained from the three glucose meters were calculated using the following equations:

$$Sensitivity = \frac{TruePositives}{TruePositives + FalseNegatives}$$

$$Specificity = \frac{TrueNegatives}{TrueNegatives + FalsePositives}$$

$$PositivePredictiveValue = \frac{TruePositives}{TruePositives + FalsePositives}$$

$$NegativePredictiveValue = \frac{TrueNegatives}{TrueNegatives + FalseNegatives}$$

RESULTS
A total number of 206 subjects were recruited into the study. Out of the 206 subjects, 130 (63.1%) were males while 76 (36.9%) were females. Most of the subjects were under 5 years (63.6%) with the mean age of 3.95 ± 3.68 years.

Packed Cell Volume (PCV) of the subjects
The mean PCV for the subjects was 26.3 ± 7.4%, range: 9.0 to 48.0%. Most of the subjects (62.6%) had PCV below 30%.

Descriptive statistics of the blood glucose results by the various methods
The mean blood glucose for laboratory method, Accu Check Active, On Call Plus and One Touch Ultra Mini were 5.67 ± 1.66, 5.87 ±1.67, 7.03 ±2.24, and 6.05 ±1.76 mmol/l respectively. All the three glucose meters had negative bias with highest mean error recorded by on call plus (Table I). The MARDs for Accu-Chek Active, OneTouch Ultra Mini and On Call Plus were 11.58%, 13.91% and 27.00% respectively.

Table I:Descriptive statistics of the blood glucose results generated by the various methods.

Variables	Accu-Chek Active	On Call Plus	OneTouch UltraMini	Reference Laboratory
Mean	5.87	7.03	6.05	5.67
Std Deviation	1.67	2.24	1.76	1.66
Std Error of Mean	0.12	0.16	0.12	0.12
Minimum	0.60	1.10	1.10	0.80
Maximum	13.50	15.10	13.00	12.80
Mean difference/error	-0.19	-1.36	-0.39	-
Correlation coefficient (r)	0.89	0.80	0.87	-
Coefficient of Variation	0.28	0.32	0.29	0.29
MARD (%)	11.58	27.00	13.91	-

Blood glucose values in mmol/l.

The Predictive Indices of the three Glucose meters in detecting Hypoglycaemia and Hyperglycaemia
Four out of the 206 subjects had hypoglycaemia confirmed by the reference laboratory method. Only three out of the four cases of hypoglycaemia were detected by all the three glucose meters and misdiagnosed one. So they all had equal predictive indices in detecting hypoglycaemia. The summary of the predictive indices of the three glucose meters in detecting hyperglycaemia is shown in Table II. Eighteen out of the 203 subjects had hyperglycaemia confirmed by the reference laboratory method. All the glucose meters had good sensitivity in detecting hyperglycaemia. Although, Accu-Chek Active had the lowest sensitivity of 83.3% but it had the highest PPV of 68.1%. The On Call Plus had the lowest positive predictive value of 30.4%. All the glucose meters had high specificity and NPV with the On Call Plus having the lowest specificity of 79.3%.

Table II: Sensitivity and Specificity of the three glucose meters in detecting Hyperglycaemia (summary)

Variables	Accu-Chek Active	On Call Plus	OneTouch Ultramini
Sensitivity	83.3%	94.4%	94.4%
Specificity	96.3%	79.3%	94.7%
Positive predictive value	68.1%	30.4%	62.9%
Negative predictive value	98.4%	99.3%	99.4%

DISCUSSION
In this study three commonly used glucose meters in our children emergency room were objectively and independently evaluated for accuracy by comparing their glucose values with the concurrent glucose results from our hospital laboratory. These glucose meters utilize different analytical principles or techniques (reflectometry, electrochemical and biosensor).They also use two different enzymes (Glucose oxidase and Glucose

dehydrogenase). The three glucose meters use fresh capillary blood but they were calibrated to display plasma-equivalent glucose values.

Using the full range of blood glucose values measured in this study, Accu Chek Active blood glucose values were the closest to that of the hospital central laboratory compared to the other two glucose meters. It reported results with the lowest MARD, mean difference and lowest coefficient of variation. The mean blood sugar level of results produced by Accu Chek Active was also the closest to that of central laboratory.

The performance of OneTouch UltraMini closely followed that of the Accu Chek Active based on the calculated MARD, mean blood glucose, mean difference and coefficient of variation values. Although the results of these two glucose meters appeared to be very close by using these technical parameters, it is very important to note that the magnitudes of these differences could be clinically significant especially where the blood glucose values could change treatment decisions in a situation requiring precise glucose measurement.

On Call Plus had the highest MARD which was more than twice the MARDs for the other two glucose meters and also had the highest mean blood glucose value and the largest mean difference. Hence, the On Call Plus glucose meter tended to generate blood glucose values that were higher than the laboratory method and the other two glucose meters. Physicians in children emergency room must use the result of On Call Plus glucose meter with caution in making diagnosis and taking therapeutic decisions. In doing these, laboratory confirmation is advised to prevent wrong therapeutic intervention.

It is pertinent to observe that all the three glucose meters evaluated, on average, tended to overestimate blood glucose values compared to the reference method as depicted by their negative mean difference. This may be explained by the high prevalence of anaemia in the patients studied as majority of the subjects (62.6%) had a PCV below 30% which is below the recommended PCV range for the three glucose meters.Haematocrit abnormalities (anaemia and polycythaemia) have been demonstrated on some meters to have an inverse effect on glucose meter results; that is, patients with anaemia can have falsely high readings and patients with polycythaemia can have falsely low readings.

In the detection of hyperglycaemia, the On Call Plus and OneTouch UltraMini were more sensitive than the Accu-Chek Active but Accu-Chek Active had the highest PPV and On Call Plus had the lowest PPV. For every 10 cases of hyperglycaemia diagnosed by the On Call Plus glucose meter only 3 were true positive. This poses a great danger in the use of this glucose meter by individuals living with diabetes for self-blood-glucose-monitor at home and for adjusting insulin doses based on the readings of the glucose meter. Also using the On Call glucose meter in the emergency room may lead to wrong diagnosis of hyperglycaemia with attendant wrong medical interventions.

The OneTouch UltraMini glucose meter was more sensitive than Accu-Chek Active in detecting hyperglycaemia but slightly lower PPV. OneTouch UltraMini diagnosed 9.4 cases out of every 10 cases of hyperglycaemia diagnosed by the laboratory method, whereas Accu-Chek Active detected 8.3 cases out of the 10. However, Out of every 10 detected cases of hyperglycaemia, Accu-Chek Active and OneTouch UltraMini glucose meters had 6.8 and 6.3 cases as true positive respectively. Hence, in clinical situations where hyperglycaemia is envisaged, the use of OneTouch UltraMini is better.

Looking at the specificity of the glucose meters in detecting hyperglycaemia, the Accu-Chek Active had the highest specificity (96.2%), followed by OneTouch UltraMini (94.6%) while On Call Plus had the least specificity (78.9%). All the glucose meters had high NPV (Accu-Chek Active 98.9%, On Call Plus 99.3%, and OneTouch UltraMini 99.3%).The high specificity and a high predictive values of Accu-Chek Active and One Touch UltraMini means that a negative result can be relied upon as being truly negative.

There were only 4 cases of hypoglycaemia detected by the laboratory method in this study and 3 of the cases were correctly detected by the three glucose meters. Although, this number was small and might not be sufficient to draw any significant inference, a study done by Oyenusi et al in a children emergency room of a tertiary hospital with a larger number of subjects withhypoglycaemia reported a similar sensitivity(75%) for Accu-Chek Active glucose meter. A brand of glucose oxidase based- glucose meter (Prestige IQ) evaluated by Elusiyan et al in a children's emergency room of a tertiary hospital in Ile-Ife reported a higher sensitivity (96.0%) compared to the 75% reported for the two glucose oxidase based glucose meters (One Touch Ultra Mini and On Call Plus) evaluated in this study.

Glucose meters are commonly and widely used in diverse settings including home care by diabetic patients, in the clinics and emergency care units. Important therapeutic interventions are based on the results of the glucose meter. It is therefore important that glucose meter values are accurate and precise as failure in this regard may lead to critical medical errors. The 3 glucose meters evaluated in this study varied in their accuracy compared to the laboratory method. Hence, it is necessary for glucose meters to be evaluated before use, and the specific meter model selected should be based on its performance in the intended patient population and environment.

CONCLUSION

The three glucose meters evaluated varied in accuracy.

The On Call Plus glucose meter tended to generate blood glucose values that were higher than the laboratory method and the other two glucose meters.

In the detection of hyperglycaemia, the On Call Plus and OneTouch UltraMini were more sensitive than the Accu-Chek Active but Accu-Chek Active tended to be more reliable.

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