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Performance Evaluation And Analytical Comparison Between Glucose Meters And Spectrophotometric Methods For Blood Glucose Determination

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Abstract: *Analytical methods comparison for the determination of blood glucose are essential in clinical laboratory practice as it improves the quality of health care through accurate and reliable clinical decision making. This study was done to assess the analytical performance between the Glucose meters and spectrophotometric methods for blood glucosedetermination.The Glucometer method determined glucose by using the Finetest Auto-coding™ Premium(infopia Co., Korea) and was compared with the spectrophotometer(Kenza 240,biolabo france) using paired data of blood samples analysed respectively from208 patients in the hospital.Data analysis was performed using Analyse-it ® Version 4.6 method validation software. The results shows that the mean value of blood glucose concentrationswere higher in by the spectrophotometric method KENZA 240 (5.76 mmol/l) than by the FINE TEST glucose meter (5.27 mmol/l).Result of t-test analysis revealed a statistically significant difference (p<0.05) between the pairs of overall measurements by the two methods. Pearson's analysis revealed a high correlation value (r = 0.946) between KENZA 240 and FINE TEST measurements of blood glucose. Passing-Bablok fit of the regression line provided the equation: FINE TEST (mmol/l) = -0.3071 + 0.9821 KENZA 240 (mmol/l); and slope value (0.9821, 95% CI: 10.9375 to 1.023) supports the high correlation coefficient. The Bland-Altman plot of mean difference expresses high level of agreement between the KENZA 240 and FINE TEST measurements.This studyconcluded that the glucose meters are sufficiently reliable for clinical decision making.*

Keywords: *Spectrophotometer,Bloodglucose,Glucose meter, hyperglycemia, hypoglycemia*

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I. Introduction

Glucose is quantitatively the most abundant carbohydrate that exists in the circulation of mammals and serves as the principal fuel for peripheral tissues except during prolonged fasting [1].Glucose levels in the blood may be transiently increased as a result of the absorption of ingested glucose from the gut.The liver enzyme glucokinasefacilates the rapid removal of large quantities of glucose from the portal vein after a meal, preventing the renal threshold for glucose(approximately 10mmol/L) being exceeded and causing unnecessary glycosuria[2].

The blood sugar concentration or blood glucose level is the amount of glucose (sugar)present in the blood of a human or animal[1].The body naturally tightly regulates blood glucose levels as part of metabolic hemeostatis[3]. With someexceptions glucose is the primary source of energy for the body cells and blood lipids in the form of (fats and oil).Glucose levels are usually lowest in the morning, before the first meal of the day (termed "the fasting level"), and rise after meals for an hour or two by a few millimole.A high level of blood glucoseoutside the normal range is referred to hyperglycemia,while low level is hypoglycemia,then diabetes mellitus is characterized by persistent hyperglycermia[5]. Alcohol-induced hypoglycaemia should be regarded as a separate case in that there is a specific biochemical reason for the hypoglycaemia(i.ealcoholinhibits gluconeogenesis)and its occur in normal as well as well as in disease liver[5].Neonatal hypoglycaemia has been defined as a blood concentration below 1.10mm/L in the preterm or low birth weight infant,below1.67mmol/l from birth to 72hrs, and below 2.22mol/L thereafter in the fullsized or full term infant[6].Thedetection,identificationandquantification of glucose in blood has played a vital role in the diagnosis and management of patients suffering from disorder of carbohydrate metabolism and is is one of the most frequently performed determinations in clinical chemistry[1].

In Nigeria and mostly in the northern part of the country, diabetes is on the increase due to diet (mostly carbohydrate) and lifestyle.The development of self-monitoring of blood glucose is probably the most important

advance in controlling diabetes since the discovery of insulin in the 1920s and provides the ability for diabetes patients to test their own blood glucose and adjust insulin dosage to control their glucose needs[7].Glucose meters have now found a wide range of applications in medicine both for diagnostic purposes in identifying hypoglycemia and hyperglycermia in the emergency room and physician's office and for managementof tight glycemic control in in intensive care units[8].For accuracy determination,glucose levels from the same specimen would ideally be compared by analysis on the glucose meter and by reference or comparative method[8].There are physical differences between the glucose concentration in serum/plasma and a whole blood as well as venous compared to capillary.Glucose equilibrates into the aqueous portion of a blood sample.the concentration of water in serum/plasma differs from the concentration of water in the cellular portion of the blood,erythrocyte contain lipid membranes and high levels of hemoglobin protein that exclude water[9].so the water content of a specimen will vary based on the the hematocrit(erythrocyte percentage).Serum/plasma thus has a higher water content and therefore higher glucose concentration by approximately 11-12% compared to whole blood at a normal hematocrit of 45%[9].

II. Materials And Methods

2.1. Study Setting and Design

The study was carried out at the chemical pathology laboratory of the Benue StateUniversityTeaching hospital makurdi.This studywas conducted from November 2015 toOctober 2016.A total of208 patients were randomly sampled at the Benue State University Teaching Hospital,Makurdi during the study period. The study was approved by the Health Research and Ethics Committee of the Hospital.

2.2. Determination of Blood Glucose

The two methods were compared for blood glucose determinations, they include the strip glucose meter method using the Finetest Auto-coding™ Premium (infopia Co., Korea), blood glucose monitoring system and the spectrophotometric method by KENZA 240TX (Biolabo, France).A total of 208 samples were analysed, and blood glucose was determined through the spectrophotometric method by measuring 1mL of the reagent to 10mL of the sample, and then incubated for 10 minutes at a temperature of 37 °C, the sample was inserted into the analyzer and the results read-off. Blood samples were placed on the glucometer strip and read.The spectrophotometric method involve the principle of glucose been oxidised by glucose oxidase to gluconic acid and hydrogen peroxide which in conjugation with peroxidase reacts with chloro-4-phenol and 4-amino antipyrine to form a red quinoneimine.glucose oxidase were glucose is oxidised by glucose oxidase to gluconic acid and hydrogen peroxide [10].

D- glucose +O_2 -> D-gluconic acid + H_2O_2

2.3 Statistical analysis

Data collected were collated on Microsoft Excel spread sheet and analysis was done using Analyse-it ® Version 4.6,(Analyse-it Leeds,UK)[11] A p-value of less than 0.05 ($p < 0.05$) was considered significant.The software supports the latest CLSI and industry-recognised protocols, enables the analyst to validate, verify and demonstrate analytical accuracy, precision, linearity, reference intervals, and diagnostic performance[11]

III. Results

A total of 208 subjects were sampled and 416 paired data were obtained and analysed in this study.The results shows that a Bland-Altman error plot illustrated that >5.6mmol/l. (62.2%) data points were positive; indicating that KENZA 240 measurements overestimated FINETEST.The results (shows Table 1) that the mean value of blood glucose concentrations were higher in by the spectrophotometric method KENZA 240 (5.76 mmol/l) than by the FINE TEST glucose meter (5.27 mmol/l).Result of t-test analysis revealed a statistically significant difference ($p<0.05$) between the pairs of overall measurements by KENZA 240 and FINE TEST.Sensitivity/specificity analysis with the receiver operating characteristic (ROC) curves (Figures 3 and 4) was performed to determine relevant cut-off values that indicated 100% sensitivity for detecting high fasting blood sugar (FBS) -glucose concentration: FBS >5.6mmol/l. The results revealed that at >5.6mmol/lKENZA 240 and FINE TEST provided 100% sensitivity (Area under the Curve - AUC = 95.0%) was 62.2% and 98.50 specificity.Pearson's analysis (Figure 1) revealed a high correlation value ($r = 0.946$) between KENZA 240 and FINE TEST measurements of blood glucose. Passing-Bablok fit of the regression line provided the equation: FINE TEST (mmol/l) = -0.3071 + 0.9821 KENZA 240 (mmol/l); and slope value (0.9821, 95% CI: 10.9375 to 1.023) supports the high correlation coefficient. The Bland-Altman plot (Figure 2) of mean difference expresses high level of agreement between the KENZA 240 and FINE TEST measurements. The average error in evaluating blood glucose with FINE TEST compared with evaluation with KENZA 240 (calculated by FINE TEST – KENZA 240) ranges between 3.24 to 8.90 mmol/l) (95% CI = -0.554 to -0.431).

Table 1:Descriptive statistics of blood glucose by methods.

Statistics	FINE TEST (mmol/l)	KENZA 240 (mmol/l)
Minimum	3.10	3.37
Maximum	8.80	9.00
Mean	5.27	5.76
Mean SE	0.095	0.098
SD	1.11	1.15
Variance	1.23	1.31
Skewness	0.7	0.7
Kurtosis	0.43	0.66

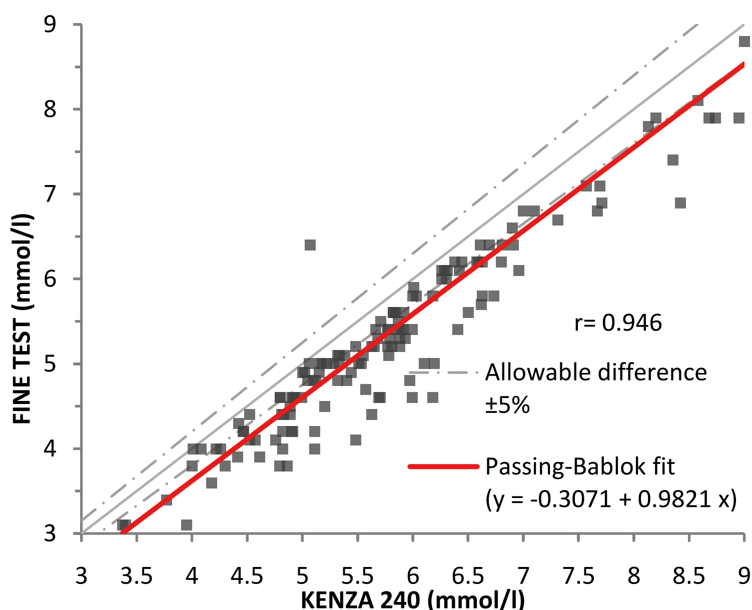

figure1: Pearson's correlation plot for Glucose

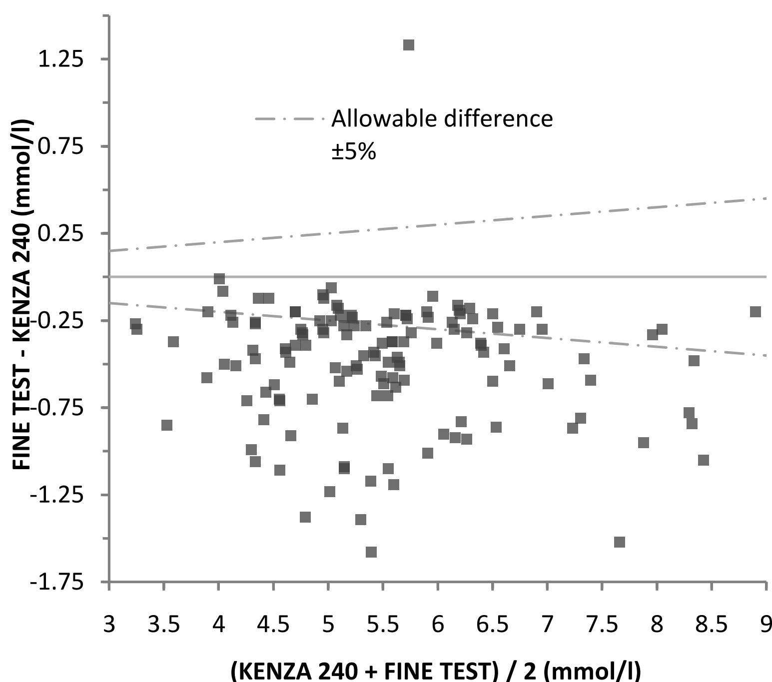

Figure 2: Bland-Altman plot comparing Kenza-Finetest Measurements

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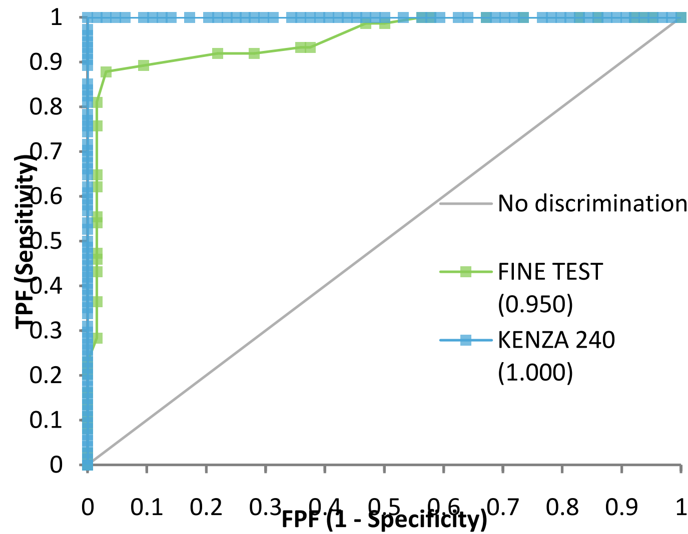

Figure 3: Receiver operating characteristic (ROC) curve for Kenza measurements at > 5.6mmol/l

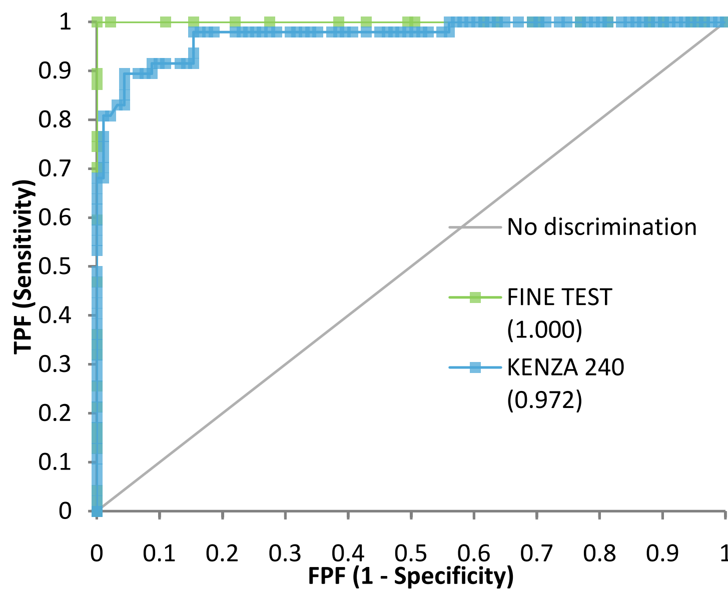

Figure 4: ROC curve for Finetest measurements at > 5.6mmol/l

IV. Discussion

The positive Bland-Altman error plot >5.6mmol/l. (62.2%) indicated that KENZA 240 measurements overestimated FINETEST.The results shows that the mean value of blood glucose concentrations in(table1)were higher in by the spectrophotometric method KENZA 240 (5.76 mmol/l) than by the FINE TEST glucose meter (5.27 mmol/l). The Finetest Auto-codingTM Premium Blood Glucose Monitoring System is plasma-calibrated to allow easy comparison of results with laboratory methods. Blood glucose test meter which is calibrated against a whole blood method may have different results in comparison to Finetest Auto-codingTM[12].

Glucose meters are universally utilized in the management of hypoglycemic and hyperglycemic disorders in a variety of health care settings. Establishing the accuracy of glucose meter, however is challenging. Glucose meter can only analyze the whole blood and glucose is unstable in whole blood[12].Erythrocyte metablolizeglucose,so glycolysis will decrease glucose concentration[12].Result of t-test analysis revealed a statistically significant difference ($p<0.05$) between the pairs of overall measurements by KENZA 240 and FINE TEST.Pearson's analysis (Figure 1) revealed a high correlation value ($r = 0.946$) between KENZA 240 and FINE TEST measurements of blood glucose. Passing-Bablok fit of the regression line provided the equation: FINE TEST (mmol/l) = -0.3071 + 0.9821 KENZA 240 (mmol/l); and slope value (0.9821, 95% CI: 10.9375 to 1.023) supports the high correlation coefficient. It is well recognised that the colorimetric /spectrophotometric estimation of plasma glucose using glucose oxidase method is the gold standard for glucose estimation[13].However, many diabetic patients find it difficult to go all the way to the laboratory for repeated blood sugar estimation.glucometers then is mainly used by many patients,but clinicians are more concerned with

clinical agreement of the glucose meter with a serum/ plasma laboratory result [14].Acceptable criteria for clinical agreement vary across the range of glucose concentrations and depend on how the result will be used in screening or management of the patient. A variety of factors can affect glucose meter results including operating techniques, environmental exposure and patient factors[15]The Bland-Altman plot of mean difference expresses high level of agreement between the KENZA 240 and FINE TEST measurements. The average error in evaluating blood glucose with FINE TEST compared with evaluation with KENZA 240 (calculated by FINE TEST – KENZA 240) ranges between 3.24 to 8.90 mmol/l) (95% CI = -0.554 to -0.431.This results is in agreement with the results of many other studies[15,16,17].Clark and associates tried to address clinical agreement by developing an error grid analysis method that evaluates the clinical significance of the glucose meter result against a comparative method[17].Clinical accuracy of the instrument also depends on how the obtained information will be used,screening,diagnosis,management[18].A significant positive bias of <10 was seen in more than a third of glucose results fromthree new plasma-calibrated blood glucose meterswhen compared to another method.Glucose meter variability or precision also contributes to differences in glucose meter analytical and clinical agreement[14].A study by Boyd etal Monte Carlo simulation model,evaluated the clinical significance of glucose meter precision[19].the study reveals that pairs of meter measured and true laboratory glucoses were ramdomly generated based on a mathematical model of total glucose meter error.paired-differences were assessed for clinical accuracy against an algorithm for insulin dosing.With a glucose meter analytical variability of only 5%,clinical insulin doses varied in 8-23% of cases,depending on the glucose concentration when compared against doasgebased on the laboratory results[20]. The brain account for 60% of the glucose utilization, so infants and small children have higher glucose utilizations rates and are more prone to hypoglycemia. Standard organisations and professional societies differ on accuracy acceptability criteria. The American Diabetes Association has recommended that glucose meter s agree to within ± 15% of the laboratory method at all concentrations, with a future performance goal of ± 5% agreements at all concentrations [16] since meter performance can change across the range of the glucose concentrations, some performance criteria differ between the hypoglycemia range and hyperglycemia range. For instance, the international organization for Standardization and the US food and drug Administration has set accuracy criteria at ± 20mg/dl (1.1 mmol/l) for levels < 100mg/dl (5.6 mmol/ liter) or levels > 100mg/dl (5.6 mmol/liter) for atleast 95% of results [20].Low pH < 6.95 falsely decreases glucose readings, while high pH increases meter reading for meters utilizing glucose oxidase. In diabetic keto acidosis, glucose readings are obtained by all meters affected and display falsely decreased results[21].The results(figure3,4) revealed that at >5.6mmol/lKENZA 240 and FINE TEST provided 100% sensitivity (Area under the Curve - AUC = 95.0%) was 62.2% and 98.50 specificity.Medications taken by a patient may interfere with their glucose meter readings [21].Tang and associates studied the interference of 30 drugs with glucose meter readings [22] Glucose – oxidase based meters were affected most frequently possibly because of the peroxide reduction detection method utilized by these meters. Acetaminophen and ascorbic acid consume peroxide which results in lower blood glucose. There are newer amperometric meters with a third electrode that minimized the interference[23].

V. Conclusion

Conclusively,both patients and doctors need a certain level of confidence in the results of glucose meters, with the high level of agreement between the spectrophotometric method and glucose metersmeasurements by the the Bland-Altman plot of mean difference reveals that the glucose meters are as reliable as the spectrophotometric method for blood glucosedetermination,though,pre-analytical variables should be taken into consideration when interpreting blood glucose results.This study showed the clinical accuracy of the glucose meter and concluded that the glucose meters are sufficiently reliable for clinical decision making.

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