



Comparison of Blood Glucose Values Using Two Glucose Meters and Standard Laboratory Method in Hospitalized Patients in a Teaching Hospital

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ABSTRACT

Background: Diabetes mellitus is a chronic disease with a worldwide prevalence and its complications can be prevented with close monitoring of blood glucose. Quality of blood glucose monitoring utilizing glucometers in Iranian hospitalized patients has not been well published in the literature. We evaluated the accuracy and consistency of the results of two devices compared with the standard laboratory method used for measuring glucose levels in a teaching hospital.

Methods: In this study 100 patients with the average age of 57.5 ± 17.7 years were randomly selected from 19 wards and their blood glucose were simultaneously measured using Accu-Chek Active[®](1) and Cleverchek[®](2) (commonly used in the wards) and the conventional laboratory method. Calibration was performed on both devices.

Results: Absolute Mean Difference of the devices 1 and 2 from the laboratory values were 24.3 ± 2.4 , and 38.5 ± 4.5 , respectively ($P: 0.003$). Correlation coefficient of the obtained values by glucometers 1 and 2 with lab, were 0.82 and 0.52, respectively. Calibration of the devices showed that device 1 was the most consistent device with the laboratory values, and Pearson correlation coefficient between the obtained values as a result of four reiterations for each sample in each device showed that the highest coefficient belonged to the device 1 and the least belonged to the device 2 used in the Ear, Nose, and Throat Departments.

Conclusion: The device 2 used in different wards of the hospital must be calibrated periodically. Furthermore, the device 1 generated closest results to the ones obtained through the laboratory.

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Introduction

Diabetes mellitus is a chronic disease with a worldwide prevalence. According to the prediction of the experts

in World Health Organization (WHO), the prevalence of diabetes type 2 in Iran in 2025 would be 6.8 percent equivalent to 5,215,000 people (1). In order to reduce the complications of this disease or to delay it and also to lower the treatment costs, it is necessary to regularly measure blood glucose levels (2-4) and manage the patient accordingly. Self Monitoring Blood Glucose (SMBG) has been the mainstay of diabetes management in community and hospital setting. In the hospital, glucometers are used

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to measure the blood glucose quickly and give a rapid feedback to the physician for taking appropriate actions.

Blood glucose monitoring for patients hospitalized in Al-Zahra (S. A.) Hospital in Isfahan is mainly carried out by nurses using a glucometer (Cleverchek®). Ensuring the accuracy of devices used in the inpatient setting to make appropriate clinical decisions is of outmost importance (5-7).

In the recent years, conflicting results have been reported with regard to the accuracy of these devices. A study in France, evaluated the accuracy of five different glucometers and the results showed that their accuracy was low (8). While both Goldstein and Chan reported in their research that the accuracy and efficiency of the devices were high (9-10), one study in Iran showed in consistency regarding the accuracy of the different glucometer devices (11).

Glucometers are widely offered in the market in various brands, and unfortunately despite the increasing use of these devices, setting the standard for their correct use has been controversial (12-15). With the introduction of these devices, a competition-driven development in both meter and strip technology has occurred allowing for greater accuracy and reliability of results. Despite the advances in technology, however, significant variation among these monitoring devices exist, leading to the development of performance guidelines by organizations such as the American Diabetes Association (ADA) and the International Standardization Organization (ISO). The ISO guidelines recommend that the total analytical error of the glucometers be within ± 15 mg/dl of the laboratory blood glucose concentrations when values are < 100 mg/dl. For laboratory values equal or above 100 mg/dl, the allowable analytical error for glucometers should be within 15%. When comparing the ISO to the ADA guidelines, the ADA recommends an analytical error of $\leq 5\%$ across all levels. Also, more than 95% of the individual glucose results measured by one glucometer must follow these criteria (16). Translating these recommendations using a laboratory value of 110 mg/dl, an acceptable meter reading according to the ISO criteria would be between 93.5 and 126.5 mg/dl; however 104.5 to 115.5 mg/dl is deemed acceptable according to ADA. It seems that ADA guidelines are more restrictive than ISO guidelines with regard to the glucometer accuracy. Also, it is important to note that the above guidelines have changed throughout the time as technology has improved. Therefore, comparing results of articles which have been published in different years should be done carefully keeping this into consideration.

The accuracy of blood glucose estimation using venous blood with glucometers designed for capillary sample testing has been questioned. In addition, concern has also been raised about the accuracy of capillary blood glucose estimation in the face of systemic illness, and it has been

suggested that in such patients, venous sampling may be more accurate (17).

Given the importance of proper management of hospitalized diabetic patients, careful assessment of the glucometers used in different wards of Al-Zahra Hospital (AZH) seems vital. As a part of a larger study, the accuracy of two glucometers, Accu-Chek Active® (1), used by the researcher, and Cleverchek® (2), used daily by the wards, at AZH were compared to the standard laboratory test. Also calibration of the two devices and the laboratory test were measured and compared. It should be noted that previously published studies all done outside of Iran has shown superior accuracy of Accu-ChekActive® and based on this evidence we chose to compare it with the glucometer used routinely in AZH (18-20).

Methods

This was a prospective single centre study performed in Al-Zahra, the University Hospital affiliated with Isfahan University of Medical Sciences between January and April 2013. Each participant gave informed consent, and the study was approved by the local ethics committee in Al-Zahra Hospital. For both phases, inclusion criteria were defined as any adult inpatient or outpatient who was above 18 years of age with diabetes mellitus or impaired glucose tolerance according to current guidelines. Exclusion criteria included the presence of any coagulation disorder, lack of suitable veins for blood sampling and inappropriate physical or psychological states. The study was performed in two phases on inpatients and outpatients. Following devices were used: Accu-Chek Active® glucometer (manufactured in Germany, device 1) and Cleverchek® (manufactured in Taiwan, device 2). They will be described later in the methods section.

Phase (I): In this phase, 100 hospitalized patients were randomly selected from 19 wards in AZH regardless of presence of hyperglycemia. Sample size was calculated based on the following formula:

$$\frac{(z_1 + z_2)^2 s^2}{d^2} = n$$

In the above formula n stands for the sample size. Z_1 is 1.96 for 95% confidence interval; z_2 is 0.84 for $\beta=0.8$; s is 0.7 for standard deviation of difference blood glucose values of two devices; and d is margin of error which is 0.3 s. Given above numbers, the sample size comes to a minimum of 88 individuals. We rounded up this number to 100 individuals to enhance our accuracy.

After receiving patient written consent, one random capillary blood glucose sample measured by each glucometer (1 and 2) was compared with the third sample measured by the laboratory.

In each selected ward of the hospital, 5 hospitalized

Table1. Characteristics of glucometers 1 and 2*.

System	Name	Model	Measuring Method	Enzyme	Blood Sample	Sample size (μL)
1	Accu-Chek Active®	GC	Electrochemical	GO	C,V,A,N	1-2
2	Cleverchek®	TD-4230	Electrochemical	GO	C,V,A,N	0.7

*GO: Glucose Oxidase; C: Capillary; V: Venous; A:Arterial; N:Embryonic

patients were randomly selected. The randomization was done by choosing odd numbered beds and if the samples were not enough, from the beginning of the list, the even numbers were added till number 95 was reached. In one of the wards, ICU-4, we decided to test the new Cleverchek® device which was purchased after our initial measurement of that ward in order to make comparison between the old and the new device.

Blood samples were taken from capillary of index finger of each patient by a trained researcher and measured by Accu-Chek Active® glucometer (manufactured in Germany, device 1) and Cleverchek® (made in Taiwan, device 2) and the values were recorded (Table 1). At the same time, brachial blood samples were taken from the same individuals and transported to the hospital laboratory. These samples were measured by Auto-analyzer (Hitachi 717, Boehringer Mannheim, Germany) utilizing Pars Kit strips (made in Iran). Within one to two hours of sample collection, laboratory measurements were performed and the results were recorded. Blood glucose levels less than 40 mg/dl and more than 500 mg/dl read by glucometers were repeated by the researcher.

Phase (II): In the second phase, calibration of four devices (device 1 vs. devices 2 in ENT, Endocrinology, and ICU-4 wards) was performed on a total of forty patients (ten outpatients for each device) and with four repetitions for each patient.

The obtained blood glucose values by the two glucometers were sometimes less or more than laboratory values in an equal distance, preventing us from algebraically adding them together. Therefore, the absolute value (interval) differences were used. In other words, analysis of the data was done on the mean of absolute values (ABS) of capillary blood glucose measured by the two glucometers and the laboratory values.

ABS = Absolute Value

ABS1: ABS. Lab-Accu-Chek = |Bs.lab-Bs. Accu-Chek Active®|

ABS2: ABS. Lab-Ward = |Bs.lab-Bs. Cleverchek®|

The closer the ABS values to zero, the closer the values obtained are to the laboratory results.

It is of interest to note that the calibration on the old and new device 2 at ICU4 was performed after the unfavorable results of the earlier phase were reported to the nursing staff. The researcher performed phases 1 and 2 (calibration) with the new device, the results of which were found very different.

Statistical analysis

Values are expressed as mean \pm SD. Continuous variables were tested for significant differences by two-tailed t tests or ANOVA.

The data were analyzed using paired t-test (we had one group of patients comparing mean blood glucose values obtained by two different glucometers), Pearson correlation analysis (correlation between two quantitative parameters), linear regression test, one-way variance analysis (one-way ANOVA), used for comparing mean values among several groups, LSD¹ post hoc test. All statistical analyses were conducted using SPSS version 20 (SPSS Inc., Chicago, IL, USA) and significance was defined as P value of less than 0.05.

Results

In phase 1, 53 males and 47 females were included in this analysis. The mean age was 57.5 ± 17.7 years. In phase 2, 4 males and 36 females were studied with an average age of 40.5 ± 20.3 years.

Phase 1: Average of ABS1 and ABS2, were respectively 24.3 ± 2.4 , and 38.5 ± 4.5 and paired t-test analysis showed that the two devices differed significantly ($P: 0.003$). Meanwhile, the correlation coefficient of the obtained values by glucometers 1 and 2 were respectively 0.82 and 0.52.

The linear equation in each device is shown:

1) Line 1: $Y_1 = 7.443 + 0.822X_1$

2) Line 2: $Y_2 = 82.66 + 0.359X_2$

Y_1 = Laboratory glucose value, X_1 = Accu-Chek Active® glucose value

Y_2 = Laboratory glucose value, X_2 = Cleverchek® glucose value

Figures 1 and 2 represent a linear equation for each device.

The findings are presented in Table 2, the least and highest means of ABS 2 were related to the Endocrinology and ICU-4 Wards, respectively. Also, the mean ABS 2 findings for the ICU4 (ICU4-New) are shown in this table.

Phase 2: Table 3 shows the Calibration of the devices. Mean ABS1 and ABS2 values in comparison to each other were as follows: device 1 < device 2-New ICU4-Ward < device 2 Endocrinology Ward < device 2 ENT Ward.

Pearson correlation coefficients among the values obtained from four repetitions of each test by each device

1. Least Significant Difference

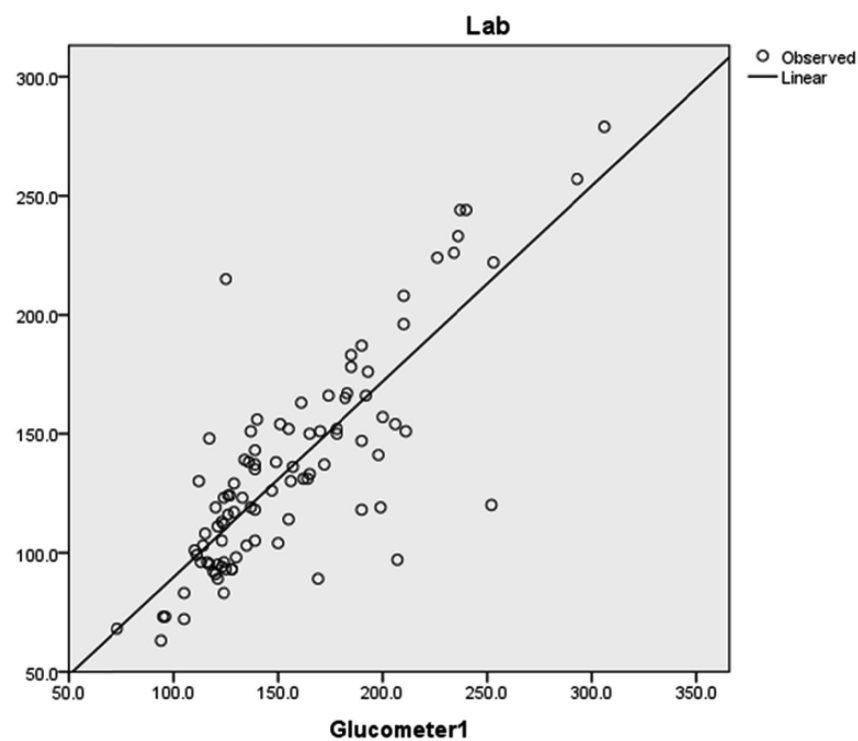


Figure 1. Curve 1 corresponds to the linear equation.

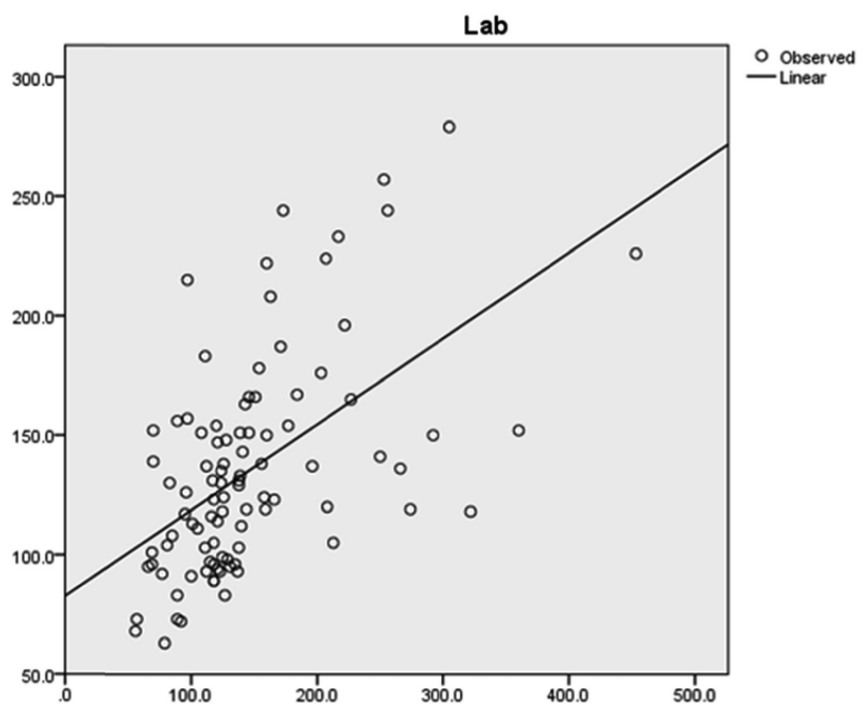


Figure 1. Curve 2 corresponds to the linear equation.

Table 2. Average blood glucose ABS2 for separate wards.

Ward Name	Sample Numbers	Mean	Standard Deviation (SD)
CCU	5	15.20	7.79
Endocrinology(Endo)	5	13.0	9.05
ENT	5	30.40	7.86
Gastroenterology	5	18.80	9.78
ICU(1&3)	5	45.20	56.66
ICU2	5	46.80	36.23
ICU4-Old	5	121.00	99.14
ICU4-New	5	38.20	26.79
Infectious Diseases	5	47.60	44.74
Internal medicine	5	27.60	24.72
Men Orthopedics	5	22.20	11.16
Men Surgery	5	42.20	38.82
Nephrology	5	16.40	11.61
Neurosurgery	5	39.00	39.54
Neurology	5	25.60	20.91
Plastic Surgery	5	46.80	31.82
Pulmonary	5	22.60	16.41
Thorax	5	72.20	75.02
Urology	5	23.40	15.85
Women Orthopedics	5	56.60	59.18
Total	5	38.55	44.40

CCU: Cardiac Care Unit; ENT: Ear, Nose, Throat; ICU: Intensive Care Unit

showed the least correlation coefficient by device 1 ($r=0.997$), device 2 in Endocrinology Ward ($r=0.974$), device 2 in ENT Ward ($r=0.345$), and the device 2-New in ICU4Ward ($r=0.909$).

The accuracy of the devices was calculated using the relation

$$\% \text{ Accuracy.glucomeler} = 1 - \text{ABS} \frac{BS_{\text{glucometer}} - BS_{\text{lab}}}{BS_{\text{lab}}} \times 100$$

This relationship was used for calibration results and the following calculations were made: Device1 (%96), devices 2 in Endocrinology Ward (90%), in ENT Ward (83%) and in New ICU4- Ward (92 %). According to ADA standard, the device accuracy should not be less than 95% (21).

In this study, DIN EN ISO 15197:2012 standard was used and was found that 100%of blood glucose results from calibration of device1followedthis standard. The results of device 2in Endocrinology Wards, 2 in ENT wards and New one in ICU4-Ward were 80%, 60% and 90% respectively.

Discussion

Management of diabetes and maintenance of blood

glucose in the recommended range is the most important way to reduce complications of this disease and reduce duration of hospitalization in hospitalized patients (22-23). Glucometers are the mainstay of blood glucose control in both community and hospital settings. Accuracy of these devices is of outmost importance. Therefore, ensuring how accurate and therefore how reliable these devices are in the daily monitoring of blood glucose became one of the goals to study by the research team.

In the present study, we showed that device 1 results had a closer correlation and lower ABS in reference to the laboratory values.

During the study, a new Cleverchek® was purchased for the ICU-4 Ward after being informed that the old device did not generate good results. Comparison of ABS between the previous and new glucometer in ICU4 ward, showed that the new device had a lower ABS and higher accuracy than the previous device (80% vs. 30%). This huge difference is a good indication that some of the glucometer devices in hospital wards may be too old, or broken, to be used and may not generate accurate results.

The results of the calibration of the two glucometers (device 1 and 2) showed that regarding the closeness of their results to the laboratory blood glucose, device 1 was

Table 3. ABS mean for each of the four devices and laboratories*.

Glucometer Name	Blood glucose values intervals by four devices and laboratories	
	Mean	Standard Deviation (SD)
1	4.98	2.3
2 Ward Endocrinology	10.02	8.1
2 Ward ENT	15.7	8.3
2 Ward ICU 4 (New)	7.5	4.8

*1: Accu-Chek Active® 2: Cleverchek®

ENT: Ear, Nose, Throat; ICU: Intensive Care Unit

significantly better than the device 2 in the 3 wards of Endocrinology, ENT and ICU4. Only device 1 followed the DIN EN ISO 15197:2012 and ADA standards. Reliability of device 1 was also superior to devices used in the selected wards as seen in the results section. It seems that device 1 provides more accurate results and is more reliable than the device 2.

In a study in Iran, Bastanhagh and colleagues have shown that the glucometers studied on 110 diabetic patients generated results differently from the laboratory standard. They compared Glucocare®, Clucotrend 2®, Glucoman® and Betacheck® with the laboratory results and all were above the 5% threshold defined by the ADA (11).

In a study in 1998 by Usmani et al., on the investigation of the accuracy of glucometer 'Q.I.D.TM3®', the results showed that more than 44% of the glucometer results compared with auto analyzer device results, revealed more than 15% difference which is against the ADA standard, and the result was not satisfactory (24).

A study in France on five different glucometer models showed that 65% of the glucometer results differed more than 10% from reference values (8).

Essack et al., assessed the accuracy and precision of five currently available blood glucose meters (GlucoPlus®, One Touch R Ultra®, One Touch R Horizon®, Accu-Chek Active®, Cleverchek® and Accu-Chek Advantage®) in South Africa. This study showed that only three of the five glucometers conformed to the ISO guidelines (GlucoPlus®, One Touch R Horizon® and Accu-Chek Active®), while none of the glucometers satisfied the guidelines recommended by the ADA (25).

A study by Daniel Sachse et al., evaluated the analytical quality and the ease of use of the Accu-Chek Mobile®. The results showed an imprecision by the standards of ADA ($\pm 10\%$) but showed an acceptable accuracy by the ISO 15197 ($\pm 20\%$) (19). Of course, the accuracy definitions by both ADA and ISO have been changed and become restrictor as time has elapsed. It appears that the definitions used in Sachse article have used the 2003 guidelines for both institutions.

Accuracy of these devices may be affected by various

factors categorized into strip, physical, patient and pharmacological factors. Strip manufacturing variances do occur even in a single device. In addition, strip storage, and expired strip scan be responsible for errors in reading blood glucose. Physical factors such as the rate of oxygen in the samples (for GO² systems), temperature and height of the location and errors in working with the device by the patient, such as the coding errors of device, careless washing of hands, blood hematocrit differences that can cause serious error could be noted. Pharmacological errors which are usually small also happen as glucose oxidase seems to interfere with such drugs as acetaminophen, L-dopa, tolazamide and ascorbic acid (26).

The possibility of hand contamination of test strips for device 2 because of frequent touching (as these strips are piled in a basket outside their containers at the time of distribution among the wards in the hospital) and therefore protein deposits interfering with correct measurement of blood glucose could be a potential source of error. The time interval between sample taking and measurement of venous blood samples can contribute to false readings due to uptake of glucose by the cells in the sample and lowered amounts of measured glucose in the sample.

Conclusion

Although using glucometer devices has greatly helped daily monitoring and control of the blood glucose, it is advisable to calibrate them on a regular basis with reference to laboratory methods. Consequently, to make correct clinical decisions, utilizing both methods (glucose measurement by glucometer and standard laboratory method) are recommended. Glucometers that have been tested and proved to be more accurate should be utilized in hospital settings and periodic calibration of these devices against the laboratory results is highly suggested.

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2. Glucose Oxidase

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