Original Article

Accuracy of a Non-Invasive Home Glucose Monitor for Measurement of Blood Glucose

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Abstract

Introduction: Patients with diabetes mellitus monitor their blood glucose at home with monitors that require a drop of blood or use a continuous glucose monitoring device that implants a small needle in the body. However, both cause discomfort to the patients which may inhibit them for regular blood glucose checks. Photoplethysmogram (PPG) sensing technology is an approach for non-invasive blood glucose measurement and PPG sensors can be used to predict hypoglycaemic episodes. InChcek is a PPG-based non-invasive glucose monitor. However, its accuracy has not been checked yet. Hence, this study aimed to evaluate the accuracy of InCheck, a non-invasive glucose monitor for the estimation of blood glucose. **Methods:** In a tertiary care hospital, patients who came for blood glucose estimation were tested for blood glucose non-invasively on the InCheck device and then by the laboratory method (glucose oxidase-peroxidase). These two readings were compared. We used International Organization for Standardization (ISO) 15197:2013 (95% of values should be within ± 15 mg/dL of reference reading if reference glucose <100 mg/dL or within ± 15% of reference reading if reference glucose ≥100 mg/dL and 99% of the values should be within zones A and B in consensus error grid), and Surveillance Error Grid for analyzing the accuracy. **Results:** A total of 1223 samples were analyzed. There was a significant difference between the reference method glucose level (135 [Q1-Q3: 97 – 179] mg/dL) and monitor-measured glucose level (188.33 [Q1-Q3: 167.33-209.33] mg/dL) (P < 0.0001). A total of 18.5% of readings were following ISO 15197:2013 criteria and 67.25% of coordinates were within zone A and zone B of the consensus error grid. In the surveillance error grid analysis, about 29.4% of values were in the no-risk zone, 51.8% in slight risk, 18.6% in moderate risk, and 0.2% were in the severe risk zone. **Conclusion:** The accuracy of the InCheck device for the estimation of blood glucose by PPG signal is not following the recommended guidelines. Hence, further research is necessary for programming or redesigning the hardware and software for a better result from this optical sensor-based non-invasive home glucose monitor.

Keywords: Blood glucose, diabetes mellitus, hypoglycemia, photoplethysmography

Introduction

Blood glucose self-monitoring can be a helpful technique in the treatment of diabetes mellitus. Patients suffering from diabetes frequently check their blood sugar levels to identify hypoglycemia and modify their insulin dosage as necessary.[1] Portable glucose monitors used for home glucose monitoring require a small drop of blood for the test whereas continuous glucose monitors have an implanted probe on the skin that senses the glucose concentration. Both of these cause discomfort among the patients. Many of the patients may not check their glucose to avoid needle pricks.[2] In addition, the device for continuous glucose monitoring is too costly for the majority of patients. Hence, research and developments are evolving for a non-invasive glucose monitor.

As the burden of diabetes is alarmingly increasing in India, mass screening at the population level is needed for early detection of diabetes for taking timely intervention to prevent or treat diabetes.[3-6] For both patients suffering from diabetes

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and screening of the population, a non-invasive glucose monitor is the dream of the healthcare system.[7] If an optimally accurate glucose monitor is available, it can screen thousands of people in a single day. In this context, research is evolving for making non-invasive glucose monitors.

The non-invasive techniques are based on a variety of methods, such as spectrometry or the examination of other variables that are connected with the glucose level. A reliable and comfortable method for real-time, non-invasive measurement of blood glucose would significantly improve treatment efficacy and help in the early detection of hypoglycemia.[8]

The use of photoplethysmography (PPG) sensor technology enables non-invasive measurements of blood glucose in a variety of environmental settings. PPG sensors are essentially optical sensors that measure variations in light absorption. Currently, this technology is utilized to measure blood pressure, heart rate, and blood oxygen saturation.[9-11] Recent research demonstrated that by analyzing heart rate variability, PPG sensors may be utilized to anticipate hypoglycemic episodes.[12,13]

InChcek (Agatsa Software Pvt Ltd., Noida, Uttar Pradesh, India) is a PPG-based non-invasive glucose monitor. This device requires a few seconds to show the blood glucose level by analyzing the PPG signal with its proprietary algorithm. This device was in the initial testing phase where the device was sold on the company website and the company collected glucose readings from the patients where patients sent reading from the device and reading obtained on their usual invasive glucose monitor.[14]

There is no literature available about the accuracy of the device when compared with plasma glucose. Hence, we designed this study to find the surveillance accuracy of the device.

Materials and Methods

Type and settings

This was a cross-sectional study to evaluate the accuracy of a non-invasive glucose monitor – InCheck. This study was conducted in a tertiary care teaching hospital situated in Jharkhand from June 2022 to December 2022.

Participant recruitment

Research participants were recruited from the central laboratory of the institution where patients came for testing blood sugar. Patients with type 2 diabetes mellitus (T2DM) were recruited in this study. They were explained about the study and recruited only after obtaining written consent for participation. Any willing patients aged >18 years were recruited. Patients with nail color, pigmentation on the finger, or any vascular disease were excluded from the study.

Auxiliary measurement

The patients were screened by a general clinical examination to rule out any obvious disease or disorder. They were also enquired about their clinical history of the disease. The duration of diabetes was also recorded. The height and weight were measured by a portable stadiometer to the nearest 1 mm and by a digital weighing scale with 100 gm sensitivity, respectively. If some patients are not found to be not following 12-h fasting, they were instructed to come the next day following a 12-h fasting for a credible fasting blood glucose level.

Measurement of glucose

On the device sensor, the participants put their fingers and after a 30 sec waiting period, the first reading was taken. Then with a gap of 30 seconds, another two readings were taken to get an average value. All three measurements and the average values were stored for further analysis.

Then the participants were tested for blood glucose from a sample of venous blood collected with aseptic precautions from the antecubital vein. The blood was collected in a commercial vial containing sodium fluoride/potassium oxalate as an anticoagulant. The blood sample was tested for plasma glucose immediately (or within 1 hour) in the central laboratory by the glucose oxidase-peroxidase (GOD-POD) method. We used an automatic biochemistry analyzer (Erba EM 200; Transasia Bio-Medicals Ltd., Mumbai, India) available in our setting.

Data analysis method

Data were presented in mean, standard deviation, median, and quartiles for observing the central tendency of the data. The distribution of the data was tested by the Shapiro-Wilk test for normality. The data were found not to follow a normal distribution. Hence, we decided to conduct non-parametric tests. For comparing the reference value and average meter value, we used Wilcoxon signed rank test. For comparing the reference values with three measurements from the glucose meters, we used Friedman's test with Dunn's post hoc analysis. For these inferential tests, we used GraphPad Prism 7 software (GraphPad Software, USA). For all the tests a $P < 0.05$ was considered statistically significant.

We used International Organization for Standardization (ISO) 15197:2013 for checking the accuracy of the glucose meter. It states that 95% of values should be within ± 15 mg/dL of the reference reading if the reference glucose <100 mg/dL or within ± 15% of the reference reading if the reference glucose ≥100 mg/dL. In addition, 99% of the values should be within zones A and B in consensus error grid analysis. Furthermore, we used the Food and Drug Administration (FDA) for checking the accuracy. It states that 95% of meter reading should be within ± 15% of reference reading and 99% of reading should be within ± 20%. A modified Bland-Altman plot was also made for a visual representation of the accuracy. For these two number-based calculations and one error grid and modified Bland-Altman plot, we used a guideline prepared by Mondal and Mondal[15] and used their free tools to generate the grid figure.

The surveillance Error Grid is a newer method for analyzing the accuracy of a glucose monitor. It is based on a similar model error grid analysis with an advanced algorithm to categorize the coordinates in the different risk zone. We have used the

online software (https://www.diabetestechnology.org/seg) for the surveillance error grid analysis.[16]

Ethical aspect

After a full review of the protocol, this study was approved by the Institutional Ethics Committee (Number: 05(C)/IEC/PJMC Dated 04/02/2022). The research participants were recruited after obtaining written informed consent.

Results

A total of 1223 pair of data was obtained from 728 (59.53%) men and 495 (40.47%) women suffering from patients suffering from type 2 diabetes mellitus. The age, height, weight, and body mass index of the research participants are shown in Table 1.

The blood sugar reading from the laboratory reference method and reading from three measurements from the glucose monitors and the average of the three readings are shown in Table 2. When we compared the reference value with the average reading obtained from the monitor, the glucose reading from the monitor was significantly higher ($P < 0.0001$) than the reference method (as tested by Wilcoxon signed-rank test). The comparison of reference values with three measurements and average values were also statistically significantly ($P < 0.0001$) higher. Among the total of 1223 measurements, the blood glucose reading of the monitor was lower than the reference glucose reading in 206, was equal in three, and was higher in 1014 measurements.

According to ISO 15197: 2013 criteria, 95% of meter reading should be within ± 15 mg/dL of reference reading (if reference glucose is below 100 mg/dL) and within ± 15% of reference reading (if reference glucose is above 100 mg/dL). We found that only 18.5% of the reading is following the criteria as shown in Table 3. Hence, the meter is not following the accuracy level suggested by ISO.

The distribution is graphically shown in a modified Bland-Altman plot in Figure 1.

In addition to number-based accuracy, the meters should also follow graph-based accuracy as per ISO. According to ISO

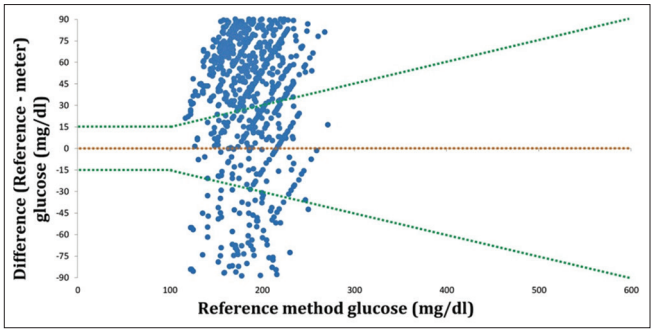

Figure 1: Modified Bland-Altman plot showing the difference between reference and meter readings in relation to reference values (according to ISO ISO 15197:2013 criteria, coordinate points between the two green dotted lines should be 95%)

Table 1: Age, anthropometric data, and duration of disease of the participants

Parameters	Mean	Standard deviation	Median	First quartile – third quartile
Age (years)	42.08	14.2	40	30-55
Height (cm)	166.87	7.46	166	160.6 – 173.4
Weight (kg)	68.65	14.33	68.5	57.5 – 81.4
BMI (kg/m^2)	24.8	5.67	24.68	20.57 – 28.79
Duration of disease (years)	3.12	1.41	3	2-4

Table 2: Blood glucose level measured by reference method and from glucose monitor

Method of measurement		Mean	Standard deviation	Median	First quartile – third quartile	*P* value of Friedman test
Reference (mg/dL)		148.15	61.62	135	97-179	<0.0001*
Glucose monitor (mg/dL)	First measurement	203.42	50.52	211	167-232	
	Second measurement	181.35	45.67	180	150-220	
	Third measurement	177.62	48.11	178	137-207	
	Average of three measurement	187.46	29.79	188.33	167.33 – 209.33	

**P* value of Friedman test (non-parametric ANOVA); in post hoc test (Dunn's test), all pairs except second and third measurement pair showed statistically significant difference

Table 3: Distribution of deviation of glucose meter reading from reference method reading

ISO 15197: 2013 criteria	Range	Number of observation	Percentage	Total percentage
Within	≤5% or 5 mg/dL	74	6.1	18.5
	>5-10% or mg/dL	60	4.9	
	>10-15% or mg/dL	92	7.5	
Beyond	>15-20% or mg/dL	49	4	81.5
	> 20% or 20 mg/dL	948	77.5	

15197:2013 criteria, 99% of the coordinates in the consensus error grid should be in zone A and B. However, 67.25% of coordinates were within Zone A and Zone B. The rest 32.75 was in zone C as shown in Figure 2. Hence, clinically, the device may not detect the glucose level with the required accuracy.

According to FDA criteria, 95% of meter reading should be within ± 15% of reference reading and 99% of reading should be within ± 20%. Hence, the meter is also far behind following the FDA criteria as 77.5% of meter glucose reading is beyond ± 20% of the reference method. Hence, the glucose monitor is not following both ISO and FDA criteria.

The surveillance error grid analysis is shown in Figure 3 and the risk category is shown in Table 4. About 29.4% of values were in the no-risk zone, 51.8% in slight risk, 18.6% in moderate risk, and 0.2% were in the server risk zone.

Discussion

With an aim to find the accuracy of the device – InChcek, we found that the device does not meet the minimum criteria set by ISO or FDA. Hence, using this device may not provide clinically acceptable blood glucose levels. Patients and physicians should use a device that helps to detect any high or low blood glucose levels in an emergency. In addition, routine checks and dose adjustments of insulin also need glucose monitor. Patients with diabetes need to prick their fingers to get blood for testing by currently available glucose monitors. In addition, mass screening of the population is cumbersome with a device that requires pricking the fingers. Hence, a non-invasive optical sensor-based glucose monitor may be the game changer. However, the device that was available in India to consumers did not meet the required accuracy for usage in home blood glucose monitoring.

Non-invasive blood glucose is based on analyzing acoustic waves, microwaves, electrical, and optical signals. PPG analyzes the optical signals. Blood glucose has different absorption rates of different lights and these data are used to calculate the blood glucose.[17] A previous study showed that GlucoTrack can detect blood glucose from the ear lobe with clinical accuracy. However, this device is not available to Indian consumers.[18] Several technologies have emerged for non-invasive glucose monitoring from different sites like the forearm, wrist, oral cavity, and earlobe with technologies like spectral analysis of light pathway of tissue, optical signals, using artificial neural network, infrared-based models, and image and convolutional neural network.[19] However, the monitoring systems are not accurate for clinical decision-making.[20]

The study has a limitation regarding the reference method. The suggested reference for measuring the accuracy of the glucose meter is the isotope dilution mass spectrometry method. However, we used the GOD-POD method that is a field method of glucose estimation. These field techniques are commonly used in laboratories in developing nations to assess blood glucose. We did not have access to the actual reference method and used the GOD-POD method for reference. Furthermore,

Table 4: Surveillance error grid risk category wise distribution of pairs

Risk level	Risk category	Number of pair	Percentage
0	None	360	29.4
1	Slight, lower	313	25.6
2	Slight, higher	320	26.2
3	Moderate, lower	200	16.4
4	Moderate, higher	27	2.2
5	Severe, lower	3	0.2

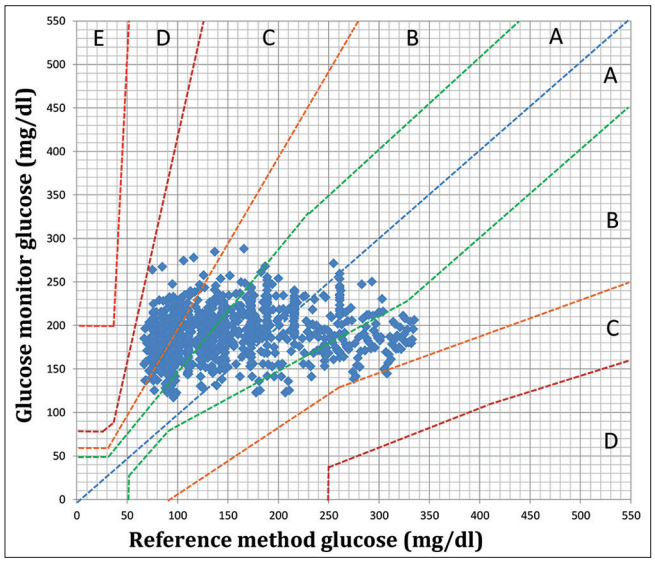

Figure 2: Consensus error grid analysis by using coordinates generated from reference and meter glucose reading

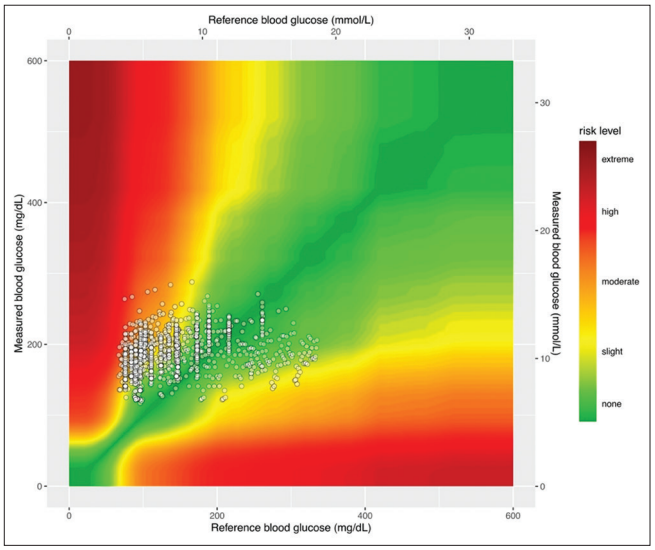

Figure 3: Surveillance error grid with plotted coordinates generated from reference and meter readings

although the non-invasive method is being developed and tested for glucose estimation, there is no separate guideline for measuring the accuracy of these devices. Hence, we used the most frequently used method – ISO for testing the accuracy of the meter.

Conclusion

The accuracy of the InCheck device, a non-invasive glucose monitor for the estimation of blood glucose by PPG signal is not following the recommended guidelines of accuracy. The meter did not meet both the FDA and ISO criteria for surveillance accuracy. Patients and clinicians should always check the accuracy level before start using a device or suggest a device to patients. We presume that further research is necessary for programming or redesigning the hardware and software for a better result from this optical sensor-based non-invasive home glucose monitor.

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Conflicts of interest

There are no conflicts of interest.

Authors contribution

HM: Concept, Design, Analysis, Visualization, Interpretation of data, and Drafting of manuscript.
SKB: Data acquisition and Review draft critically.
NP: Interpretation of data and Review draft critically.
SM: Concept, Interpretation of data, and Review draft critically.
All the authors approved the final version of the manuscript to be published and agreed to be accountable for all aspects of the work.

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