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Non-invasive Glucometer using Acetone Gas Sensor for Low Income Earners' Diabetes Monitoring

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Abstract: A glucometer is an important device used to monitor blood glucose level of diabetes patients to prevent degenerated health conditions. The conventional glucometers are characterized by piercing of the sample site for patients' testing. The invasive nature of these glucometers is painful to the patients and some patients are also scared at the sight of blood. To promote glucometer acceptance among patients, it is important to develop a non-invasive glucometer using acetone gas sensor with "exhaled breath" collected non-invasively as the sample for the glucometer. After the device development, exhaled breath sample of twenty subjects with age range of 20 to 55 years from a University were taken using the developed acetone sensor device. Prior to the exhaled breath sample collection, the blood glucose levels of the volunteered subjects were also determined using the conventional and proprietary invasive clinical method. To infer whether there is significant different between the mean of the results obtained from the conventional and the exhaled breath method, a t-test was carried out on the results and *P* values of 0.9860 and 0.9306 were obtained for fasting blood sugar and random blood sugar respectively, indicating no significant differences in the results obtained from the developed device when compared with the proprietary device. Hence, non-invasive glucometer using acetone gas sensor can be used to promote inexpensive personalized diabetes monitoring without inflicting pain on the patients. Promotion of this device could also reduce the expenses incurred on lancet and test strips, thus, making it suitable for low income earners.

Keywords: Acetone Sensor, Glucometer, Non-invasive

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1. INTRODUCTION

Glucometer is the device used for regular monitoring of the blood glucose level. Blood glucose monitoring is very important for the management of patients suffering from both Type I diabetes mellitus (TIDM) and Type II diabetes mellitus (TIIDM). This device provides real time measurement [1] and also enables patients to make right decisions on food intake, the nature of physical activities to be engaged with and when to seek medical interventions especially in each time the hyperglycemia threshold is exceeded or when the glucose level is below the threshold-hypoglycemia [2]. This regular monitoring may reduce the risk of degenerated health issues such as stroke, heart attack and nerve damages [3, 4].

Physiologically, there are numerous cells in the body, these cells perform metabolic functions efficiently when there is adequate secretion of insulin from the pancreas into the blood stream in the presence of blood glucose which is the major source of energy [5-8]. The purpose of the insulin is to unlock the channel on the cell through which glucose flows into the cell [5]. This process of unlocking is achieved when insulin binds with the insulin receptor on the cell [9]. The major causes of TIDM and TIIDM are lack of insulin secretion by the pancreas and impaired insulin receptor [10]. The effect of this is an increase in the blood glucose level of the patient due to the absence of insulin in the blood stream and the locked glucose channel on the cell [10]. Another effect of impaired insulin secretion is increase in ketone level in the process of ketosis, in which the fat stored in the liver is broken down for energy, thereby fat is converted to ketones. At this state, there is need for regular monitoring of the blood glucose level to avoid further health challenge that may lead to cerebrovascular disease such as stroke [11].

Exhale breath through the mouth contains many compounds in various proportions. These compounds include [11] oxygen (16%), carbon dioxide (5.3%), nitrogen (79%), water vapour (6.3%), argon (1%) and parts per million (ppm) of hydrogen, ammonia, isoprene and acetone. Isoprene and acetone are volatile organic compounds (VOC) and their presence in breath indicates certain health challenges [12]. Acetone, in particular has a fruity smell which indicates the presence of sugar, in a subject with no underlying health condition the range of breath acetone concentration lies within 0.3ppm and 0.9ppm and for a diabetes patient it could exceed the threshold of 1.8ppm [13].

Among the clinical tests that can be conducted for a diabetes patient, random blood sugar (RBS) test and the fasting blood sugar test (FBS) are the most common [14, 15]. These two tests are conventionally taken by pricking the patient's finger in order to express blood sample to be used for the test [16].The RBS test is taken regardless of the last meal time, while a FBS test is taken after an

overnight fast or fasting at least eight hours before the test. For the conventional glucometer usage, a blood sugar level of 200 mg/dl and above indicates the presence of diabetes when the RBS test is taken, while a blood sugar level of 100 mg/dl and above indicates the presence of diabetes when the FBS test is taken [17].

For the implementation a non-invasive glucometer using near infrared spectroscopy techniques [18], an infrared sensor and photodiodes have been used [19]. This design has been achieved using the principle of near infrared (NIR) in which light is transmitted to the tip of the finger [19] which is the measuring site. The intensity of the light scattered in this medium could normally be converted to an electrical voltage value through the exposure detector and coefficient reflection spectrum analysis. Thereafter, the voltage value was transmitted to the microcontroller where the amount of the blood glucose was estimated using the prediction algorithm [19].

Evidence in the literature indicated several research attempts to implement non-invasive glucometer [20], this involves the use of various techniques such as reverse near infrared spectroscopy [18], absorbance spectroscopy [21], iontophoresis [21-25], bioimpedance spectroscopy [26, 27], thermal emission spectroscopy [29-31] and metabolic heat conformation (MHC) theory [18]. One method of non-invasive glucometer's development employed by Takeuchi et al. [31] applied metabolic heat conformation (MHC) theory [18] based on machine learning. This method used machine learning to classify the presence or absence of diabetes based on skin and ambient temperature of the patient. This method recorded 80% accuracy of predictive classification; the effect of change in body temperature used may be due to other factors besides diabetes. Moreover, this method did not state the exact blood glucose value which could aid clinical management of the affected patients.

Wang et al. [32] also developed a non-invasive glucometer using breath analysis prototype for the detection of acetone in a single breath sample. The response time of their device was 20 seconds, this from the report, is the time taken from breathe inhalation to the production of result on the screen. For this current design the period of continuous exhalation into the mouth piece was tested for both 15s and 20s, it was observed that the reading were similar, hence the 15sec time was adopted as it makes the developed system faster. The breath duration less than 15s will reduce the accuracy of the result as the microcontroller has been programmed to calculate average ppm in the breath for the duration of 15s. Furthermore, in their report, a breath sample, acetone exposure of 1.8 parts per million (ppm) was adjudged as an indication that a patient was diabetic and the light emitting diodes (LED) only comes on when the level of acetone sensed is 1.8ppm. Their developed device had no OLED screen to display the level of acetone sensed, in this case prediabetes patients will not be able to monitor and manage their glucose level through breath until it reaches the advanced stage of 1.8ppm, and then the LED comes on. In this present study, our developed device has an OLED screen which displays the acetone level; this enables patients to make right decisions on food intake, the nature of physical activities to be engaged with and when to seek medical interventions.

Typically, acetone gas sensor is a nanostructure sensor [33] which uses acetone as a biomarker in the diagnosis of DM, especially the Type I DM [32]. The concentration of acetone in exhaled human breath normally falls within the range of 0.2ppm to 2.0ppm, where 1.8ppm is set as diabetes diagnosis threshold [5]. During a selected ion flow tube mass spectrometry (SIFT-MS) analysis [34], the concentrations of the common breath metabolites ammonia, acetone, isoprene, ethanol and acetaldehyde in the breath of five subjects over a period of 30 days was carried out. The mean concentrations, in parts per billion (ppb), of each metabolite range amongst the five subjects included ammonia, 422– 2389; acetone, 293–870; isoprene, 55–121; ethanol, 27–153; acetaldehyde, 2–5 [34].

In another study by Tayyab et al., (2018)[1] the acetone concentration in breath was measured using MQ 138 sensor, samples of one hundred patients were collected from local hospitals in Pakistan. The blood glucose levels of these patients were determined using conventional invasive clinical method as a comparison to MQ 138 sensor report. A trained linear regression classifier was used to map the breath acetone level to the collected blood glucose level. Although a good correlation of 0.92 was reported in their work but it did not investigate distinctly the performance of their proposed device for both the FBS and RBS states. This suggested the need for additional study on improvement to this device for effective use in low resource settings. Hence, in this present work, the performance of the developed device was investigated in comparison to the proprietary glucometer while implementing the FBS and RBS states. Our study has uniquely put into consideration the t-test results for FBS and RBS tests in order to compare and ascertain consistency in accuracy. The device developed by Tayyab (2018) did not ascertain the accuracy of its device using these two important states (FBS and RBS).

The purpose of this study is to develop a non-invasive glucometer that will eliminate pain [35], trypanophobia and homophobia which are experienced through the use of invasive glucometer. This will also save cost incurred on lancet and test strips in proprietary glucometers. Because for the conventional glucometer, the test strip alone costs about 16.32USD for 25 strips, while Lancet costs 9.67 USD. Over time, once the patient runs out of these items, he/she will incur expenses on them and may even be financially incapable to purchase them. Take a home with more than one diabetes patient, the expenses could be too outrageous for the low-income earners. Thus, our developed device is suitable for this category of patients. The cost analysis for the developed device is shown in Table 1. The device was developed using acetone sensor MQ 138 and ADUINO UNO Atmega 132. It is true that MQ138 sensor is sensitive to many other compounds e.g Toluene, Ethanol and Formaldehyde. These compounds that MQ138 are sensitive to are not major constituents of human breath. Hence, it can only measure the concentration of acetone with high precision as other components are usually not present or present in very insignificant quantity. For this design it is strongly advised that the device should be used when not on alcohol. Besides, the reading taken during the eight (8) hours fasting period could have eliminated the effect of

alcohol.

Table 1. Analysis of cost for the device

S/NO	MATERIALS	UNIT(S)	PRICE / UNIT PRICE (USD)	TOTAL PRICE (USD)
1	Arduino Uno	1	9.67	9.67
2	MQ138	1	34.82	34.82
3	LCD	1	4.84	4.84
4	Battery 1.7A, 3.7V (Lithium-ion)	1	2.42	2.42
5	Plastic package	1	4.84	4.84
6	Jumper wire	75	0.18	7.26
7	Memor\\y card module	1	4.84	4.84
	Amplifier Module	1	2.06	2.06
8	Bulk Converter	1	3.14	3.14
	LED	2	0.05	0.1
9	Push Buttons	3	0.24	0.73
	Speakers	1	1.21	1.21
10	Vero Board	1	0.24	0.24
11	Resistor	3	0.05	0.15
	Switch	1	0.12	0.12
	GRAND TOTAL			**76.44**

2. THEORETICAL AND EXPERIMENTAL METHODS

The major components used for the construction of this non-invasive glucometer are: MQ-138 acetone gas sensor, lithium ion battery of 3.7 v, buck converter, microcontroller (Aduino Uno Atmega 328), SD-card module, OLED Screen and mouthpiece [20]. The microcontroller was programmed using C programming language. The programming code includes the conversion formula as stated by Tayyab et al.

$$Acetone\ concentration = \left(-2.6*\log\left(\frac{R}{R_o}\right)+2.7\right)^0 \quad (1)$$

Where R is the resistance (in Ohms) measured by the acetone sensor, while the R_o is 10 kOhms which is the inbuilt resistance of the acetone sensor.

The tested and validated code was then uploaded onto the microcontroller. The MQ-138 Acetone sensor has four pin-terminals[21] which are the ground pin, digital output pin, analogue output pin and supply voltage pin. The sensor was powered by the battery through the connection of the voltage supply pin to the bulk converter. The analogue and digital pins of the gas sensor was connected to the analogue and digital pins of the microcontroller respectively. The gas sensor also has its heating element which is powered through the bulk converter. The SD-card module was used for logging the measured data. This has six pin-terminals in which the voltage supply pin and the ground pin were connected onto the voltage supply and ground terminals of the Arduino board, respectively, while the remaining four pins were used for serial communication between the SD-card module and the Arduino Uno.

Light emitting diode (LED) is made up of heating filament that radiates light when electric current flows through it. The negative leads of the red and green LEDs were connected to the ground while the positive leads were connected to pins 11 and 12 on the microcontroller respectively. The circuit has been programmed to allow current flow to the red LED when the measured acetone is high and current flow to the green LED when the measured acetone is low. This is to assist illiterate patients who do not understand the results by having a light emitting diode as an indicator which indicates normal value and abnormal value of acetone.

The amplifier module was also connected to the microcontroller, the output of the amplifier was connected to the speaker which gives out a sound immediately a signal is sent to it.

The OLED screen was also powered by the Arduino for serial communication, the V_{in} and ground terminals of the screen were connected to 5V and ground terminals of the Arduino, respectively. The switch was connected to the power supply for switching the whole device on or off. Jumper wires were used to achieve connections between components. The block diagram for the construction is shown in Figure 1.

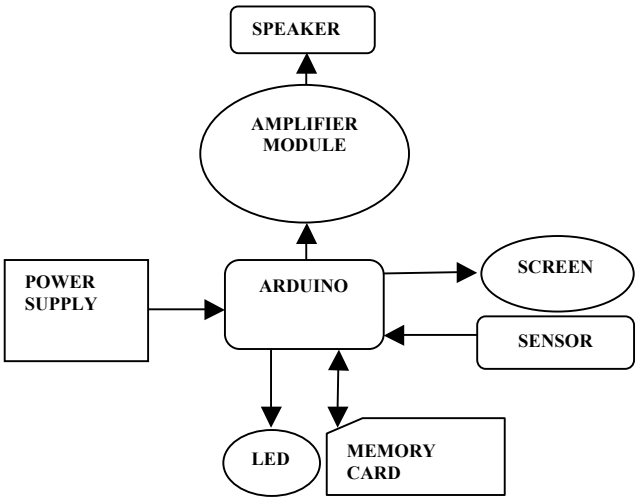

Figure 1. The Block Diagram for the Construction.

2.1 Data Collection

After the construction, written informed consent was obtained from each of the participants to be subjected to the constructed device. The participants include 10 female subjects and 10 male subjects. The experimental protocol was conducted in line with the revised declaration of Helsinki and was approved by the University's ethical review board.

The device was used to take measurement from twenty subjects of age range 20 to 55 years old in a University setting. Samples of exhaled breath were taken from these volunteered twenty subjects using the acetone sensor device. The subjects were instructed not to eat at least eight hours before the test based on the fasting blood

sugar (FBS) test condition. They were subjected to FBS test using the developed device and a conventional glucometer [5] as displayed in Figures 2 and 3. After the FBS, the subjects were given glucose drink of 50cl and allowed to rest for 30 minutes before the random sample collection tests were taken using both the constructed device and a conventional glucometer. The results from the two devices were then compared using a t-test. Specifically, performance evaluation was carried out on the developed device in comparison with the conventional invasive device through application of a t-test. The following procedures for the tests using the constructed glucometer were observed:

I. The patients were asked to breathe for 15 seconds through the mouth on a mouthpiece that was connected to the sensor.

II. Once the gas sensor was in contact with acetone particles exhaled through the mouth, the sensor resistance changed (MQ-138 was already in form of sensor module which consist of a working voltage of 5V ± 0.1V)

III. The sensor value was then sent to Arduino UNO

IV. When the system detected the gas particles drawn through the input valve into the gas room it indicated an increase in the voltage output of the sensor.

V. The microcontroller converted the output of the sensor to a reading in parts per million

VI. The output of the reading from the microcontroller was displayed on the screen in parts per million.

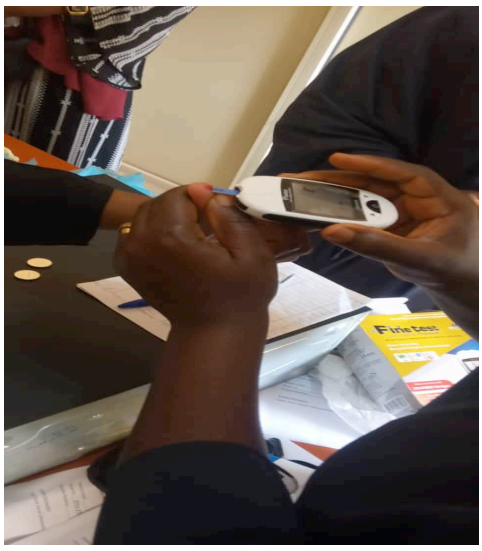

Figure 2. Testing with conventional glucometer.

Figure 3. Testing with the acetone gas sensor Glucometer.

3. RESULTS AND DISCUSSION

The results presented in Tables 2 and 3 show the FBS and RBS results of 20 subjects respectively, with 10 female subjects and 10 male subjects. The data were normalized to enhance accurate comparison and mapping as shown in Figures 4 and 5.

The threshold used for the classification of high or low blood glucose in this report is 1.0mg/dl. 1.0mg/dl below 100mg/dl is classified as normal, while 1.0mg/dl above 100mg/dl is classified as diabetics.

As shown in Table 2, while using the conventional glucometer, subjects 3, 4, 5, 7, 9, 10, 12, 17 and 18 were observed to have high glucose in their blood stream after the FBS test. The non-invasive glucometer using acetone sensor also showed this from the breath sample of this set of subjects. Table 3 showed increase in the glucose level after the consumption of glucose drink by the subjects and diabetes threshold of 1.8ppm was reached and exceeded by the same set of subjects (i.e., subjects 3, 4, 5, 7, 9, 10, 12, 17 and 18).

In order to infer the differences or similarities in the glucometer measurement reading using both the non-invasive acetone gas sensor (the device reported in the current study) and the conventional glucometer, the normalized results using both devices were subjected to t-test as well as Pearson correlation coefficient test. The t-test for the FBS had a *P*-value of 0.9860 and correlation coefficient of 0.9941, hence there is 98.6% confidence showing that results from both devices have no statistical significant differences and there is strong positive correlation between the breath acetone and blood glucose samples.

The normalized values of the RBS results were also subjected to t-test as well as Pearson correlation coefficient test. The *P*-value was 0.9306 while the correlation coefficient was 0.9932, showing that results from both devices has no statistical significant differences. Hence there is 93.06% confidence that the non-invasive acetone sensor glucometer can be used in place of the invasive glucometer because there is strong positive correlation between the breath acetone and blood glucose sample.

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Table 2. Results of Fasting Blood Sugar (FBS)

Subjects	Conventional Glucometer Readings (mg/dl)	Acetone Device Readings (ppm)	Gender	Age
1	61	0.71	F	23
2	63	0.76	F	23
3	180	1.73	F	22
4	208	2.00	F	39
5	193	1.97	F	23
6	78	0.80	F	20
7	198	2.09	F	45
8	99	1.00	F	23
9	102	1.03	M	20
10	216	2.09	M	55
11	96	0.98	F	55
12	100	1.02	F	18
13	96	0.98	M	18
14	59	0.68	M	21
15	99	1.00	M	22
16	92	0.86	M	20
17	112	1.20	M	21
18	185	1.90	M	22
19	99	1.00	M	51
20	95	0.98	M	23

Table 3. Results of Random Blood Sugar (RBS)

Subjects	Conventional Glucometer Readings (mg/dl)	Acetone Device Readings (ppm)	Gender	Age
1	84	0.95	F	23
2	122	1.24	F	23
3	198	2	F	22
4	233	2.09	F	39
5	207	2	F	23
6	135	1.45	F	20
7	241	2.3	F	45
8	105	1.09	F	23
9	107	1.15	M	20
10	228	2.25	M	55
10	228	2.25	M	55
11	126	1.3	F	18
12	118	1.16	F	18
13	135	1.45	M	21
14	89	0.95	M	22
15	107	1.15	M	20
16	104	1.07	M	21
17	132	1.34	M	22
18	197	1.94	M	51
19	103	1.03	M	23
20	108	1.15	M	21

Figures 2.3 and 2.4 show the graph of the normalized value of the FBS and RBS results using both devices. The graph shows similarities in the blood glucose level and the breath acetone level when both devices were put to use.

When the results of the proprietary glucometer were compared with the developed glucometer it showed that the t-test for both the FBS and RBS had a *P*-value of 0.9860 and 0.9306 respectively, showing that results from both devices have no statistical significant differences. While the correlation coefficient results for both FBS and RBS were 0.9941 and 0.9932 respectively. These are strong positive correlation close to what was recorded by Tayyab et al. [5].

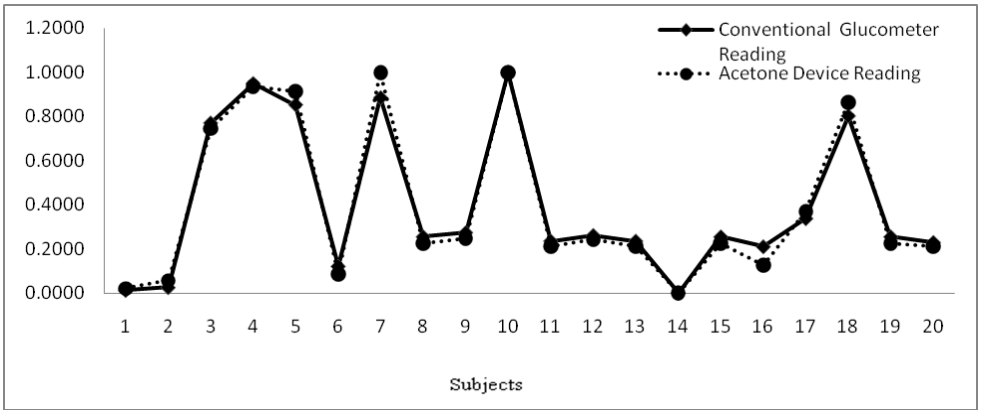

Figure 4. Graph showing similarities between non-invasive acetone sensor device reading and conventional glucometer reading for fasting blood sugar test (FBS).

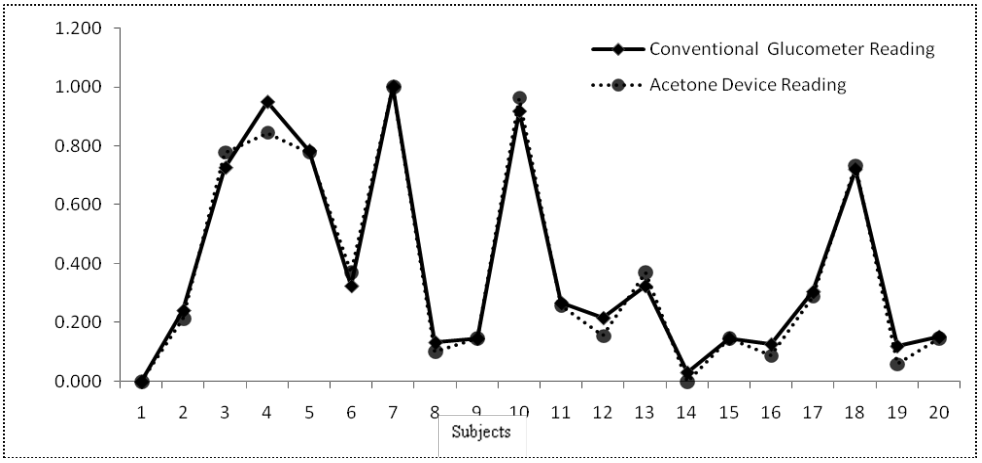

Figure 5. Graph showing similarities between non-invasive acetone sensor device and conventional glucometer reading for random blood sugar test (RBS).

4. CONCLUSION

In this paper, the non-invasive glucometer using acetone sensor was developed and subjected to performance test in comparison to the conventional and invasive glucometer. The performance test showed that the non-invasive glucometer using acetone gas sensor can be used in place of the conventional glucometer without inflicting pains on the user. Also, the use of this non-invasive glucometer allows inexpensive glucose monitoring, hence it is suitable for low income earners. In the future, there is intension to incorporate program that will allow the simultaneous display of glucose level both in mmol/L and mg/dL.

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