

The Effectiveness of Acetone Breath Content Using Chitosan Based Sensor in Patients Diabetes Mellitus

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Abstract

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BACKGROUND: The high incidence of diabetes mellitus in Indonesia to encourage researchers to continue to develop detection techniques are easy, inexpensive and minimally invasive. This study is expected to answer the challenge. Detection tool used in this research is the detection devices use traditional breath acetone levels of chitosan-based sensors. Acetone breath sensor works based on the chemical interaction between the breath of patients with diabetes and acetone sensor surface, which causes a change in the electrical response.

AIM: This study was cross-sectional using diabetes mellitus patients as research subjects by measuring breath acetone levels and HbA1c and KGD as a comparison.

METHODS: Research conducted at the primary health care facilities network services the University Hospital of North Sumatra. A total of 58 diabetic patients who meet the inclusion and exclusion criteria were included in this study. The relationship between the measurements analysed using Pearson correlation test.

RESULTS: Measurements showed that statistically there is a great relationship between breath acetone levels with or KGD HbA1c levels in the diabetic patient with each $R = 0.05$ and $p = 0.708$ for the relationship acetone breath and HbA1c and $R = 0.1$ and $p = 0.445$ for the relationship acetone breath and KGD. However, clinically there is a linear relationship between increased levels consistent acetone in the breath with increased HbA1c levels as well as levels of KGD.

CONCLUSION: Examination of breath acetone levels can be considered as an indicator of diabetes detection.

Introduction

Based on data from the World Health Organization (WHO), Indonesia is one of the contributor's patients with diabetes mellitus (DM), the largest by occupying the 4th position of the world and national causes of death in most cases 3 after heart disease and stroke (DG P3L 2010). Moreover, diabetes is not a disease that can be eliminated but can only be controlled so that the condition does not worsen. This fact is enough to conclude that prevention and early detection of diabetes is one step that absolutely must be done to curb the high prevalence of diabetes, especially in Indonesia.

Up to now has been a lot of testing done related to the early detection of diabetes. One of the testing using a blood sample *glucometer*. Although this method seems practical, testing of blood samples is considered invasive, painful; Accuracy remains low and relatively expensive. Likewise with HbA1c, although the DM detection method has high accuracy in measurement but is very expensive and not portable. Therefore, people mostly have to go to health institutions to know their blood sugar levels when not able to have a tool like Glucometer check blood sugar or HbA1c.

These deficiencies addressed with DM through the breath detection method that tends to *non-invasive*, Painless, more practical with a short

analysis time and is relatively inexpensive. Breathing method is a new method that does not exist conducted to analyse diabetes by analysing the blown gas released through the patient's mouth [1].

Health report showed that high levels of glucose encourage the formation of acetone. Acetone is one of the outputs produced by diabetics through the breath that has a higher concentration than healthy people. The concentration of acetone in the range of 0.3 ppm s / d 0.9 ppm was found in healthy human breath while in the breath of people with diabetes could reach 1.8 ppm [2]. Things need to be done in analysing the breathing is a detector that has very high sensitivity and presented online and in real-time.

Chitosan is *conductive biopolymer*. Very interesting to study as a new sensing material that is sensitive to acetone because it contains many amino groups (-NH₂) and hydroxyl (OH) in the molecular structure. These groups provide sites for bonding active molecules of acetone to interact and cause changes to the electrical conductivity of chitosan. Besides, by maintaining the value of its pK, a ~ 6.5 Chitosan becomes soluble in acidic aqueous media that allows chitosan is deposited in the form of a thin film onto a substrate by electrodeposition method. Special advantages owned by chitosan is believed to lead to great success to produce acetone breath sensor that has high sensitivity, response time is faster and cheaper.

Based on the above matters, so in this study will be conducted using the breath acetone concentration detection sensor chitosan-based in DM patients were controlled and uncontrolled that is expected to replace the detection method using Glucometer blood sugar levels and HbA1c can match detection methods.

Material and Methods

This study is an observational study using a cross-sectional design (cross-sectional). The study was conducted in health care networks First Level University Hospital of North Sumatra. When the study is from March to October 2018. The target population was all patients with Diabetes Mellitus in Medan. The samples are all patients with Diabetes Mellitus who meet the inclusion and exclusion criteria.

All study subjects had requested her consent after an explanation of the purpose of the study, methods of sampling and research benefit from the researchers.

Approval of the study has been issued by the Health Ethics Committee of the Faculty of Medicine, University of North Sumatra.

Procedure

Factual testing procedures of chitosan-based sensors is done by testing patients with DM with acetone breath; they exhale into the sensor system. Furthermore, patients with DM will be tested her blood sugar levels using a glucometer and blood samples taken last them to be tested in the laboratory HbA1c levels.

Results

During the period from March to October 2018, to obtain samples such as blood sugar levels, HbA1c and acetone levels in the breath of people with diabetes in the Diabetes Clinic and Clinic Alifa Telkom in Medan. Total obtained 58 samples that meet the criteria for inclusion in this study (Table 1).

Table 1: Percentage KGD diabetic patient by Category Low, Borderline, High and Very High

Category	Total	Percentage
Low	6	10.3
Borderline	15	25.9
High	19	32.8
Very High	18	31.0
TOTAL	58	100

The table above shows that the percentage of people with diabetes are at KGD High category (32.8%). Average Blood Sugar Levels was 186.5 ± 83.8 (standard deviation).

Table 2 shows that the percentage of people with diabetes HbA1c values is in the High category (62.1%). Mean HbA1c was 9.33 ± 2.1 (standard deviation).

Table 2: Percentage of HbA1c in a diabetic patient by Category Normal, High and Very High

Category	Total	Percentage
Normal	5	8.6
High	36	62.1
Very high	17	29.3
TOTAL	58	100

Table 3 above shows that the percentage of DM patient's breath acetone levels is in the High category (89.7%). The mean Acetone (chitosan) is 368.24 ± 33.5 (standard deviation).

Table 3: Percentage of breath acetone levels in a diabetic patient by Category Normal, Low and High

Category	Total	Percentage
Normal	2	3.4
Low	4	6.9
High	52	89.7
TOTAL	58	100

Table 4 shows that the in DM patients breath acetone levels are found higher in line with higher

HbA1c levels (62.06%). Statistical test using the Spearman correlation test showed that acetone (chitosan) with HbA1c very weak with $R = 0.05$ and $p = 0.708$.

Table 4: Distribution Breath Acetone Levels of HbA1c levels compared with patients with DM

Category KGD		Categories Acetone			Total
		Normal	Low	High	
borderline	borderline	1	1	13	15
	Low	0	0	6	6
	Very high	1	1	16	18
	High	0	2	17	19
Total		2	4	52	58

Table 5 shows that the in DM patients found higher breath acetone levels in line with the high levels of KGD (32.76%). Statistical test using the Spearman correlation test showed that acetone (chitosan) and KGD very weak with $R = 0.1$ and $p = 0.445$.

Table 5: Distribution of breath acetone levels compared to levels KGD DM patients

Category HbA1C		Categories Acetone			Total
		Normal	Low	High	
Normal	Normal	1	1	3	5
	Very high	1	1	15	17
	High	0	2	34	36
Total		2	4	52	58

Table 6 shows that the in DM patients found that high levels of KGD not always followed by high HbA1c levels. Found there are 17% of patients with high HbA1c levels, but the levels of KGD borderline. Statistical test using the Spearman correlation test showed that HbA1c and KGD are strong with $R = 0.7$ and $p = 0.01$.

Table 6: Distribution of HbA1c levels compared with the levels of KGD DM patients

Category hba1c		Borderline	Category KGD			Total
			Low	Very high	High	
Normal	Normal	3	1	0	1	5
	Very high	2	1	11	3	17
	High	10	4	7	15	36
Total		15	6	18	19	58

Discussion

Based on data from this study, it appears that the average blood sugar levels in the diabetic patient were 186.5 ± 83.8 (standard deviation). The mean Acetone (chitosan) is 368.24 ± 33.5 (standard deviation) and the mean HbA1c levels were 9.33 ± 2.1 (standard deviation). This is in line with the distribution of blood sugar levels, acetone breath and HbA1c showed that all of these parameters indicate a high category for each variable. It is clinically proven that we see that there is a linear relationship between the synergistic or three parameters. In Table 5 is shown that almost all patients with diabetes who have high

levels of acetone breath then the patient HbA1c levels are also high. Although the levels are not always followed by an increase in blood sugar levels. This indicates that the clinical measurement of breath acetone levels following higher HbA1c levels than KGD. Therefore, according to researchers acetone breath can be used as a detector that can represent the levels of HbA1c. Still, before deciding whether the examination of acetone breath can be used in place of HbA1c, you should do more research to examine the levels of acetone in the blood for each subject were examined levels of acetone breath. In this research shows that there is a weak correlation between breath acetone levels with HbA1c or KGD. This is probably due to the number of samples that are still considered insufficient.

However, at least we see there is a connection even if the relationship is weak. For that, we need to do further research by increasing the number of samples. Therefore, according to researchers acetone breath can be used as a detector that can represent the levels of HbA1c. Still, before deciding whether the examination of acetone breath can be used in place of HbA1c, you should do more research to examine the levels of acetone in the blood for each subject were examined levels of acetone breath. In this research shows that there is a weak correlation between breath acetone levels with HbA1c or KGD. This is probably due to the number of samples that are still considered insufficient. However, at least we see there is a connection even if the relationship is weak.

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One interesting finding in this study is that although the statistically weak association between variables visible but clinically, we see that the relationship between variables is strong enough.

We can conclude:

1. Average Blood Sugar Levels DM patients were 186.5 ± 83.8 (standard deviation);
2. The mean HbA1c in the diabetic patient was 9.33 ± 2.1 (standard deviation);
3. The mean Acetone (chitosan) DM patients was 368.24 ± 33.5 (standard deviation);
4. Correlation acetone (chitosan) with HbA1c in diabetic patient is very weak with $R = 0.05$ and $p = 0.708$;
5. Correlation acetone (chitosan) and KGD diabetic patient is very weak with $R = 0.1$ and $p = 0.445$;
6. Correlation of HbA1c and strong enough KGD DM patients with $R = 0.7$ and $p = 0.01$;
7. Although statistically, the correlation test acetone breath on HbA1c and KGD showed a very weak but clinically shown that there is a consistent linear relationship between increased levels of

acetone in the breath with increased HbA1c levels as well as levels of KGD.

References

1. Directorate General of Disease Control and restructuring Lingkungan. Measurement Technical Guide Risk Factors for Diabetes Mellitus. MOH. Jakarta, 2008.
2. Irwan Sofia, Word and Zulfiana Haris. Characterization of physicochemical and functional chitosan derived from tiger shrimp shell waste. *Journal of Chemical Engineering Indonesia*. 2010; 9(1):11-18.
3. Kun-Wei Kao Ming-Che Hsu, Yun-Hwa Chang, Shangjr GWO, J. Andrew Yeh. A sub-ppm acetone detection gas sensor for diabetes using ultra-thin 10 nm thick Inn FETs. *Sensors*. 2012; 12:7157-7168. <https://doi.org/10.3390/s120607157> PMID:22969342 PMCid:PMC3435971
4. Nasution TI, Nainggolan I, Hutagalung SD, Ahmad KR, Ahmad ZA. The sensing mechanism and detection of low concentration acetone using chitosan-based sensors. *Sensors and Actuators B: Chemical*. 2013; 177:522-8. <https://doi.org/10.1016/j.snb.2012.11.063>
5. IT Nasution, Asrosa R, Machrina Y, Nainggolan I, Balyan M, Rumansyah R. Improved Electrical Properties of Chitosan-Based Sensor by Adding Acetone Carboxymethylcellulose (CMC). *IOP Conference Series: Materials Science and Engineering*. 2017; 180:012-018. <https://doi.org/10.1088/1757-899X/180/1/012018>
6. Petry Motsegood and Johna Leddy. Detection on human breath acetone using cyclic voltametry. *ECS Transactions*. 2012; 41(18):1-7. <https://doi.org/10.1149/1.3684414>
7. Dutta PK, Dutta JD, Tripathi VS. Chitin & Chitosan: chemistri, properties and applications. *Journal of Scientific & Industrial Research*. 2004; 63:20-31.
8. Bansal V, Sharma PK, Sharma N, Pal OP, Malviya R. Applications of chitosan and chitosan derivatives in drug delivery. *Advances in Biological Research*. 2011; 5(1):28-37.