Perbandingan Nilai Diagnostik dari Point of Care Testing (POCT) dengan Pemeriksaan HbA1c Standar di Pelayanan Kesehatan Primer (PHC)

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ABSTRAK

Diabetes Mellitus adalah salah satu masalah kesehatan terbesar. HbA1c digunakan untuk mendiagnosis, memantau pengobatan dan penyesuaian pengobatan. Kromatografi Cair Kinerja Tinggi (HPLC) dan spektrometri massa semprotan elektron direkomendasikan untuk mengukur HbA1c. Namun kedua metode tersebut membutuhkan biaya yang mahal, fasilitas yang berpotensi menambah beban biaya kesehatan. Pengukuran HbA1c menggunakan Point of Care Testing (POCT) sedang dikembangkan di Indonesia. POCT lebih nyaman, biaya lebih terjangkau dan mudah dibawa ke pelayanan kesehatan primer. **Tujuan:** untuk menilai kemanjuran klinis POCT dibandingkan dengan pemeriksaan standar dengan HPLC. **Metode:** Merupakan penelitian potong lintang yang dilakukan di fasilitas kesehatan tingkat pertama (FKTP) di Malang. Populasi subjek adalah pasien rawat jalan di FKTP dengan kriteria inklusi berusia 20-75 tahun, merupakan peserta program penanganan penyakit kronis (PROLANIS), baik diabetes maupun non-diabetes. **Hasil:** Tiga ratus tiga puluh delapan subjek berpartisipasi dalam penelitian ini. Lima subjek dikecualikan karena adanya anemia. Kami menggunakan uji Wilcoxon untuk membandingkan kadar HbA1c antara dua metode dan uji korelasi Rank Spearman untuk menemukan korelasi antara dua metode. Hasil penelitian menunjukkan pengukuran kadar HbA1c dengan metode POCT memiliki akurasi yang baik (> 80%). Selain nilai diagnosis, peningkatan pemanfaatan POCT HbA1c mungkin juga disebabkan oleh portabilitas dan kenyamanan pasien. **Kesimpulan:** Adanya korelasi yang kuat ($R = 0,016$) antara POCT HbA1c dan pengukuran standar. POCT HbA1c juga menunjukkan akurasi yang baik pada semua kelompok HbA1c.

Kata Kunci: diabetes mellitus, HbA1c, High Performance Liquid Chromatography (HPLC), Point of Care Testing (POCT)

Comparison of Diagnostic Value between Point of Care Testing (POCT) and Standardize HbA1c Testing in Primary Health Care

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ABSTRACT

Diabetes Mellitus is one of the biggest health problems. HbA1c is used to diagnose, to monitor treatment and treatment adjustment. High Performance Liquid Chromatography (HPLC) and electron spray mass spectrometry are recommended to measure HbA1c. But both methods need expensive cost, facility, and potentially increase health cost burden. HbA1c measurement using Point of Care Testing (POCT) is developed in Indonesia. POCT is more comfortable, has lower cost and easily brought to primary health care. **Aim:** to assess the clinical efficacy of POCT compared with a standard examination by HPLC. **Methods:** It is a cross-sectional observational study conducted at a first-level health facility (FKTP) in Malang. The subject population was patients who went to an outpatient unit in FKTP with inclusion criteria aged 20-75 years, were participants in the chronic disease management program (PROLANIS), both diabetes and non-diabetes. **Results:** Three hundred and thirty-eight subjects were participated in this study. Five subjects were excluded because the presence of anemia. We used Wilcoxon test to compare HbA1c level between two methods and Rank Spearman correlation test to find correlation between two methods. This study showed measurement HbA1c level using POCT method had good accuracy (>80%). Other than diagnosis value, increased utilization of POCT HbA1c might also be caused by its portability and patient's comfort. **Conclusions:** This study showed a strong correlation ($R=0.016$) between POCT HbA1c and standardized measurement. POCT HbA1c also showed good accuracy in all HbA1c groups.

Keywords: diabetes mellitus, HbA1c, High Performance Liquid Chromatography (HPLC), Point of Care Testing (POCT)

INTRODUCTION

Diabetes Mellitus (DM) is one of the biggest health problems in the twenty-first century. At present, there are an estimated 415 million people with diabetes worldwide and 318 million people with impaired glucose tolerance that have the potential to become diabetes.^[1] Data released from the results of basic health research (RISKESDAS) show that the prevalence of diabetes in Indonesia is 5.7% while the prevalence of people with impaired glucose tolerance or who are often grouped into prediabetes is 10.2%.^[2]

The diagnosis of DM can be made by using fasting blood glucose (GDP) or blood glucose testing 2 hours after 75 grams of glucose (OGTT) or by HbA1c. These three

examinations have the same place in establishing the diagnosis of DM. ^[3,4] In addition to establish the diagnosis, blood glucose, and HbA1c checks are also important to carry out monitoring that could be used as a guide to improve management such as changes in diet / physical activity or adjusting the dose of drugs/insulin. ^[5,6]

Two large-scale studies, Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) showed that intensive therapy using HbA1C as a target can reduce the risk of developing microvascular complications. The decrease in HbA1C is identical to the reduced risk of diabetes-related complications. Data

from UKPDS shows that each 1% decrease in HbA1c, it will decrease the relative risk of myocardial infarction by 14% and the risk of microvascular complications by 37%.^[7] Besides, HbA1c examination is an indirect test to measure the average blood glucose. Several other factors can affect HbA1c such as age, race/ethnicity, the presence of anemia/hemoglobinopathy, history of blood transfusion in the last 2-3 months and disorders of kidney function.^[8,9]

Guidelines issued by the American Diabetes Association (ADA) as well as from the Indonesian Endocrinologist (PERKENI) states examination of HbA1c for diagnosis must use methods that certified by the National Glycohemoglobin Standardization Program (NGSP) and standardized by studies from Diabetes Control and Complications Trial (DCCT).^[3,4] In Indonesia, not all laboratories use NGSP standards, accuracy and caution are needed in interpreting the HbA1C examination.

High-Performance Liquid Chromatography (HPLC) and electron spray mass spectrometry are some of the methodologies that used as a reference for measuring HbA1c, still both of these checks require substantial costs, facilities and infrastructure.^[10] This indeed becomes a problem related to financing that must be issued by the country if this examination is a routine examination for diabetic patients in Indonesia.

In recent months, the HbA1c examination with Point of Care Testing (POCT) is developed in Indonesia. POCT is a method of the investigation carried out outside a central laboratory that uses tools. Some of the advantages of this POCT examination include: providing real-time results so that doctors can immediately provide motivation and management plans based on the results obtained; using capillaries

so that the patient is more comfortable; and is cheaper and easier to carry to primary health facilities.^[5, 11-14]

This POCT examination has not recommended for the diagnosis of T2DM. This examination has several shortcomings, such as the absence of evidence that states that this examination will provide better outcomes for patients, better optimize diabetes services, and improve HbA1C. Besides, standardization of the use of HbA1C is also still not available properly.^[15-19] For this reason, a study aimed at assessing the clinical effectiveness of POCT, which includes its accuracy is compare with a standard examination by the HPLC method.

METHODS

Study Design

This study is a cross-sectional observational study conducted at a first-level health facility (FKTP) in Malang. The subject population was patients who went to an outpatient unit in FKTP with inclusion criteria aged 20-75 years, were participants in the chronic disease management program (PROLANIS), both diabetes and non-diabetes. While the exclusion criteria are hemoglobin levels <10 gr/dl or hemoglobinopathy. This study was approved by Ethics committee of General Hospital dr. Saiful Anwar Malang.

Sample size

The prevalence of type 2 diabetes and glucose intolerance in Indonesia is currently 5.7% and 10.2%. An expected sensitivity level of 80% and an error rate of 5%, as many as 307 subjects need in this study.

Study procedures

The study carried out after the patient signed the consent form following this study. The patient was anamnesis and anthropometric, physical examination including blood pressure, body mass index.

Then the HbA1C POCT examination was carried out in the form of capillary blood followed by venous blood sampling to examine the HbA1C by the HPLC method. POCT examination uses Borronate affinity Tri-stat™ technology. The analysis of the HPLC method uses Premier Hb9210™. The HbA1c results grouped into three groups, namely groups with HbA1c <5.7%, groups with HbA1c ≥ 6.5%, and groups with HbA1c ≤ 7%. Complete blood tests are also performed to rule out anemia (Hb <10g / dl) and hemoglobinopathy.

Statistical Analysis

We used paired t-tests to compare HbA1c levels from the two methods or alternative statistical analysis which appropriate with types of the data. Analysis of sensitivity, specificity, positive predictive value, and accuracy. All data were analysed by computerization using Statistical Product and Service Solution software, IBM SPSS Statistics 20, with a significance level of 0.05 ($\alpha=0.05$).

RESULTS

There were 338 subjects who participated in this study. Five subjects were excluded due to anemia, resulting in a total of 333 subjects. Based on **Figure 1**, it can be seen Correlation test results showed a significant correlation between POCT HbA1c levels with standard HbA1c levels. The correlation value is 91.6% and it has positive correlation. It means that the higher the POCT HbA1c levels, the higher HbA1c levels obtained by the standard HPLC method.

Figure 1. Correlation of POCT HbA1c levels with standard HbA1c

3.1 Group of Diabetic Patient with HbA1c < 5.7 %

The results of cross-tabulation, POCT HbA1c with standard HbA1c for groups with HbA1c levels <5.7% can be seen in **Table 1**.

Table 1. POCT HbA1c levels compared to standard HbA1c levels for HbA1c < 5.7 %.

POCT HbA1c	HbA1c standard		Total
	< 5.7	≥ 5.7	
< 5.7	18	52	70
≥ 5.7	6	257	172
Total	24	309	333

*POCT, Point of Care Testing; HbA1c, Haemoglobin A1c

In this group, POCT sensitivity was 0.79, specificity was 0.99, positive predictive value was 0.98, and the negative predictive value was 0.82. The method accuracy is outstanding (0.89 / 88.89%)

3.2 Group of Diabetic patient with HbA1c ≥ 6.5 %

The results of cross-tabulation (table 2x2) POCT HbA1c with standard HbA1c for groups with HbA1c levels ≥ 6.5% can be seen in **Table 2**.

Table 2. POCT HbA1c levels compared to standard HbA1c levels for HbA1c ≥ 6.5 %.

POCT HbA1c	HbA1c Standard		Total
	≤ 6.5	>6.5	
≤ 6.5	123	38	161
> 6.5	5	167	172
Total	128	205	333

*POCT, Point of Care Testing; HbA1c, Haemoglobin A1c

Table 3. POCT HbA1c levels compared to standard HbA1c levels for HbA1c ≤ 7 %.

POCT HbA1c	HbA1c Standard	Total
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	≤ 7	> 7	
≤ 7	163	35	198
> 7	2	133	135
Total	168	165	333

*POCT, Point of Care Testing; HbA1c, Haemoglobin A1c

In this group, POCT sensitivity was 0.79, specificity was 0.99, positive predictive value was 0.98, and the negative predictive value was 0.82. The method accuracy is excellent (0.89/ 88.89%)

DISCUSSION

Overall, the results of this study indicate that the use of the POCT HbA1c examination has reasonably good accuracy (> 80%) compared to the standard examination for HbA1c. These results are the same as the study conducted by Wiwanitkit, *et al.* from Thailand who saw a correlation between the POCT HbA1c examination and with the standard HbA1c examination tool with a correlation coefficient (R) 0.99.^[19] It is not too different from our study where we obtained a correlation coefficient (R) between the two examinations amounting to 0.92. Likewise, a comparative study conducted by Sicard, *et al.* in 23 patients found a reasonably good correlation ($r = 0.76$) between the two methods used for this HbA1c examination.^[20] The same results in terms of accuracy also reported by Knaebell, *et al.* testing 3 POCT HbA1c devices at the same time compared to the standard where the correlation coefficient is 0.98, 0.99 and 0.99.^[12] In addition to diagnostic values, POCT HbA1c is increasingly used because it is more economical than standard inspection, is portable, so it is easy to be moved and used, and greater satisfaction from the patient's side.^[21,22]

CONCLUSION

The results of this study show a strong correlation ($r = 0.916$) between POCT HbA1c

and standard inspection. They also obtained useful accuracy data from the use of POCT HbA1c in all groups.

This study can be a basis for consideration of the use of POCT HbA1c in FKTP as part of the management of Diabetes Mellitus Type-2. However, it is always necessary to understand the limitations of using all diagnostic tools to avoid the results misinterpretation.

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