Research Letter

The Nanjing Glycated Hemoglobin Standardization Program: 2012 to 2015

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ABSTRACT

Purpose: This study aims to investigate glycosylated hemoglobin (HbA_{1c}), between-laboratory imprecision (%CV), and pass rates from 2012 to 2015 in Nanjing to provide evidence for improving the HbA_{1c} measurement.

Methods: This was a retrospective, descriptive analysis of HbA_{1c} levels obtained from participating hospitals in Nanjing from 2012 to 2015. The HbA_{1c} levels of fresh whole blood samples taken from healthy and diabetic adults were determined within 24 hours. HbA_{1c} levels (low level: 4.0%−6.0% HbA_{1c}; medium level: 6.1%−8.0% HbA_{1c}; and high level: 8.1%−10.0%) were grouped. Meanwhile, the target values were determined and assigned by a Level I−certified laboratory to assess the accuracy. Results as %HbA_{1c} and related detection information, such as methods, were collected from all participants, then evaluated after each survey part of the program.

Findings: Overall, the %CVs acquired by HPLC methods were lower than those determined by other methods. Pass rates ranged from 62.9% to 100%, depending on the HbA_{1c} level, and overall pass rates increased from 54.3% to 94.4% for those laboratories passing the 3 HbA_{1c} levels. In addition, the top-grade hospital-based laboratories had better performances than the secondary hospital-based laboratories in 2012 to 2015.

Implications: The use of accuracy-based proficiency testing with stringent quality-control management has greatly improved the performance of HbA_{1c} testing. The Nanjing Glycated Hemoglobin Standardization Program (NJGHSP) played an important role in this improvement by encouraging use of more rigorous quality control, participation in external proficiency testing programs, and providing education. (*Clin Ther.* 2017;39:220–229) © 2017 Elsevier HS Journals, Inc. All rights reserved.

Key words: between-laboratory imprecision, EQA, glycated hemoglobin, proficiency testing, quality control, standardization.

INTRODUCTION

Glycated hemoglobin (HbA_{1c}) is an important biochemical marker for assessing long-term glycemic control in patients with diabetes. Studies have reported on the relationship between HbA_{1c} levels and risk of development and progression of diabetic complications.[1,2] In 2010, the American Diabetes Association recommended an HbA_{1c} of 6.5% as a criterion for the diagnosis of type 2 diabetes,[3] which means that accurate determination of HbA_{1c} is even more critical. However, precision and accuracy of HbA_{1c} determination for the diagnosis of type 2 diabetes is inadequate in China because some HbA_{1c} tests are not standardized.[4] Importantly, the lack of standardization would decrease the clinical usefulness of HbA_{1c} testing, especially when different methods are used as the patients visit different physicians or health systems. The testing of HbA_{1c} is adequate for the diagnosis of type 2 diabetes in other countries (eg, the United States). Therefore, the Chinese Diabetes Association recommended that HbA_{1c} be used for diagnosing diabetes based on the improved standardization of HbA_{1c} measurements. This applies

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only to the hospitals using methods that have been NGSP certified as traceable to the Diabetes Complication Control Trial reference system or the International Federation of Clinical Chemistry and Laboratory Medicine reference method, standardized HbA_{1c} measurement and stringent quality control, with a reference range of 4.0% to 6.0% HbA_{1c}.[4] Therefore, laboratories in Nanjing were invited to participate in the Nanjing Glycated Hemoglobin Standardization Program (NJGHSP) for free in 2011. The goal of the NJGHSP was to standardize HbA_{1c} testing results so that clinical laboratory results are comparable and sufficient to meet clinical needs. Target values assigned by a NGSP Level I–certified laboratory were used to assess the accuracy since 2012. Samples were shipped to each participating laboratory once a year. The participating laboratories were asked to return all information by e-mail for statistical analysis. Feedback to participants after each survey is also part of the NJGHSP. This study aimed to evaluate the present performance of HbA_{1c} testing and the improvement in the measurement of HbA_{1c} in Nanjing and to determine whether the laboratories could pass the College of American Pathologists (CAP) criteria.[7-10]

METHODS

Samples and the Target Value

The study protocol had been approved by the Institutional Review Board of Nanjing Drum Tower Hospital. Written or verbal informed consent was obtained from the research subjects. Two milliliters fresh whole blood samples were taken from healthy and diabetic adults. All of the blood samples positive for HIV antibodies, hepatitis B surface antigen, hyperbilirubinemia, high lipids, hemoglobin variants, anemia, and hepatitis C antibody were excluded. The HbA_{1c} levels were then determined by HPLC method (Bio-Rad Variant II turbo, Hercules, California) within 24 hours.[5] A total of 30 blood samples were collected and grouped equally by HbA_{1c} levels: low level: 4.0% to 6.0% HbA_{1c}; medium level: 6.1% to 8.0% HbA_{1c}; and high level: 8.1% to 10.0% HbA_{1c}. Blood samples from each level were immediately pooled together, resulting in one pooled sample per level. Single-use 0.5-mL aliquots were prepared from each pooled sample and stored at 4°C. One aliquot from each level was chosen randomly and subsequently analyzed in triplicate by the Bio-Rad Variant II turbo; the mean of every 3 results was used as the target value.[6] The procedure was finished within a period of 3 hours. The whole blood samples made by the Level I–certified laboratory were then sent to participating laboratories within 3 hours. This procedure was repeated in 2 subsequent years. Laboratories participating in this proficiency-testing (PT) survey in Nanjing included independent laboratories, the top-grade hospital-based laboratories and the secondary hospital-based laboratories. The classification of hospitals in China is based primarily on the size, technical level, medical equipment, and management level of the hospital. Therefore, the top-grade hospitals are the best hospitals, followed by the secondary hospitals.

The clinical laboratory of Nanjing Drum Tower Hospital has been certified by the NGSP in 2013 as a Level I laboratory. The Nanjing Drum Tower Hospital was certified with the Bio-Rad Variant II turbo. In the laboratory of Nanjing Drum Tower Hospital, the %CVs of the Bio-Rad Variant II turbo and Tosoh G7 methods as measured by the day-to-day control samples with mean HbA_{1c} levels of 5.5% and 10.0% were less than 2% throughout the study period. Both methods were performed exactly as specified by the manufacturers. In addition, the measurements of samples in our laboratory have been compared with those of the samples in the NGSP Level I laboratory of Shanghai Zhongshan Hospital every quarter. Shanghai Zhongshan Hospital has been an NGSP Level I laboratory for several years. Our laboratory also attends the External Quality Assessment program offered by Bio-Rad and China National Center for Clinical Laboratory every year. All results were satisfactory.

Detection Methods

The methods are divided into 4 groups according to the analytic principles: HPLC, low-pressure liquid chromatography (LPLC), immunoassay, and boronate affinity. The HbA_{1c} analyzers evaluated in this study were: Bio-Rad Variant II, BIO-RAD DiaStat, Bio-Rad D-10, and Bio-Rad Variant II turbo (Bio-Rad Laboratories); Tosoh G7 Standard analysis mode and Tosoh G8 Standard analysis mode (Tosoh Corporation, Tokyo, Japan); ADAMSTMA1c HA-8160 and ADAMSTMA1c HA-8180 (Arkray, Inc., Edina, Minnesota); Drew DS5 (Erba Diagnostics,