Prevalence of Undiagnosed Diabetes in Patient with Random Serum Glucose Over 200 mg/dL in an Emergency Department in Korea: Preliminary Study

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Purpose: The aim of this study was to determine the prevalence of diabetes in patients with random serum glucose over 200 mg/dL in an emergency department.

Methods: A retrospective descriptive pilot study was conducted using chart review of patients who had visited the ED at Kangdong Sacred Heart Hospital. Between April and October 2014, patients aged 18 years and older with random serum glucose level higher than 200 mg/dL and having no prior diabetes mellitus (DM) were enrolled. Regardless of the patient’s chief complaint, a history of current symptoms related to diabetes of patients was obtained and additional serum HbA1c was measured. The follow-up test was recommended on endocrinology OPD or the inpatient ward. Patients’ medical records regarding diagnosis of DM were reviewed.

Results: A total of 296 patients with random serum glucose level estimated above 200 mg/dL without previous DM history were enrolled in this study, however only 82 patients were eligible. Among them, 34 patients (41.4%) were newly diagnosed as DM; 38 patients had current presumptive symptoms of diabetes while 44 patients had none of those symptoms. Twenty three patients (60.5%) with presumptive diabetes symptoms were diagnosed as diabetes while another 15 patients (39.5%) were not. Eleven (25.0%) patients without symptoms of diabetes were diagnosed as diabetes while 33 patients (75.0%) were not. The difference between two groups was significant. (p=0.001)

Conclusion: The prevalence of undiagnosed DM patients in patients with random serum glucose level over 200 mg/dL in the emergency department was considerably high. Therefore emergency physicians should pay attention to opportunistic hyperglycemia and active diabetes screening.

Key Words: Diabetes mellitus, Emergency medicine, Hyperglycemia

Article Summary

What is already known in the previous study
Current recommended tests for diagnosis of diabetes require overnight fasting plasma glucose level or a two-hour oral glucose tolerance test. However, for acutely ill patients in the emergency department, detection of diabetes using only plasma random glucose level may be burdensome and inconvenient to meet the diagnostic criteria. In addition, the serum glucose level can be easily influenced by many factors including diet, medication, and stressful conditions such as trauma. Use of HemoglobinA1c (HbA1c) in diagnosis of pre-diabetes and diabetes was recently recommended by the American Diabetes Association. In addition, HbA1c reflects recent plasma glucose state over eight to 12 weeks and high HbA1c level could indicate diabetes, being a good predictor for prevalent complications. Some studies were conducted throughout countries, except Korea, using random serum glucose level and HbA1c level for detection of undiagnosed diabetes.

What is new in the current study
The prevalence of undiagnosed DM patients in patients with random serum glucose level over 200 mg/dL in the emergency department was considerably high. Therefore emergency physicians should pay attention to opportunistic hyperglycemia and active diabetes screening.

Introduction

The estimated prevalence of diabetes mellitus (DM)
throughout the world was 8.3% of world population in 2012, which sums up to about 371 million people living with diabetes\textsuperscript{1,2}. In addition to that, the prevalence of diabetes in Asian population has increased rapidly in recent decades with a disproportionate burden in young and middle-aged individuals\textsuperscript{3,4}. Diabetes is a chronic insidious disease that develops gradually, and many individuals remain undiagnosed\textsuperscript{4}. To reduce the risk of long-term complications, the early diagnosis of diabetes is important\textsuperscript{4}. Opportunistic screening for DM during ED visit will allow initiation of appropriate lifestyle and early medication management as well as DM self-management education\textsuperscript{5}. However, adequate strategies for recognizing and managing patients with elevated glucose level in ED have still not been established yet, thus resulting the loss of opportunity for early diagnosis\textsuperscript{4,6}.

Current recommended tests for diagnosing diabetes require overnight fasting plasma glucose (FPG) level or a two-hour oral glucose tolerance test (OGTT)\textsuperscript{6,7}. However, for acutely ill patients in ED, detecting diabetes using only plasma random glucose level may be a burden and inconvenient to meet the diagnostic criteria. In addition, the serum glucose level can be easily influenced by many factors such as diet, medication and stressful conditions such as trauma\textsuperscript{7}. The use of HemoglobinA1c (HbA1c) to diagnose pre-diabetes and diabetes was recently recommended by American Diabetes Association\textsuperscript{8}. Moreover, it is well known fact that HbA1c reflects recent plasma glucose state over eight to 12 weeks and that high HbA1c level could indicate diabetes, being a good predictor for prevalent complications\textsuperscript{9-11}. In these points of view, some of studies were conducted throughout countries using random serum glucose level and HbA1c level, but not yet in Korea. Thereby we aimed to identify the prevalence of diabetes in patients with random serum glucose over 200 mg/dL in emergency department and clinical effectiveness of HbA1c\textsuperscript{2,3,12-14}.

### Materials and Methods

#### 1. Study design

We performed a retrospectively descriptive pilot study using chart review of patients who have visited ED at Kangdong Sacred Heart Hospital, an urban, university hospital which has approximately 50,000 annual visits. We enrolled people aged 18 years and older, with random serum glucose level higher than 200 mg/dL and had no prior DM, between April to October 2014. Critically ill patients, such as hemodynamically unstable, acute myocardial infarction, sepsis, mental deterioration, severe trauma, acute psychiatric illness, etc. were excluded from the study, since their clinical state might affect the serum glucose level. We also excluded the patients with acute and chronic pancreatitis, those who received intravenous glucose or systemic steroids in the past 4 weeks. In addition, patients who refused further evaluation, laboratory studies or following up for outpatient department (OPD) could not be enrolled in study.

#### 2. Study protocol

Our emergency department has a protocol about patients who have above 200 mg/dL random serum glucose level from the initial blood test, regardless of chief complaint. If the patient is identified, we check for past medical history whether the patient has been previously diagnosed with DM or the patient has present symptom associated with DM, such as polyuria, polydipsia, polyphagia and current weight loss. Then for patients with both hyperglycemia and agreed additional study, serum HbA1c level and follow-up test is recommended on endocrinology OPD or inpatient ward. We reviewed those patients’ medical records about final diagnosis of DM which done by endocrinologist decision based on laboratory result at both emergency department and additional test via OPD such as diabetes require overnight fasting plasma glucose (FPG) level or a two-hour oral glucose tolerance test (OGTT).

#### 3. Data analysis

Outcome was numbers of newly diagnosed DM patients, either via out-patient department or diagnosed during hospitalization, presented with random serum glucose level higher than 200 mg/dL in emergency department. We divided the patients into two groups, one with presumptive diabetic symptoms and others with those symptoms were absent. Then we compared the number of patients with newly diagnosed DM. Furthermore, we also compared HbA1c level in each
group. Statistical analysis were performed with PASW Statistics 18 (IBM SPSS Inc., NY, USA) and Medcalc 15.6 (MedCalc Software bvba, Belgium). Descriptive statistics were expressed by numbers and percentages or means and standard deviation (normal distribution) or medians and interquartile ranges (non-normal distribution). Comparisons of variable utilized Chi-square test (categorical variables), independence t-test (normal distributed continuous variables) and Mann-Whitney U-test (non-normal distributed continuous variables). The level of statistical significance was defined as $p<0.05$. Sample size was calculated based on the estimated prevalence of previous studies, about 14%5,6,13). With 95% confidence level and 5% precision, the required sample size was 196. Considering drop-out rates, we estimated 216 patients would be required. Therefore it would take 7 months to recruit the data, allowing for monthly frequency of hyperglycemia patient.

**Results**

During the study periods, 296 patients with estimated above 200 mg/dL random serum glucose level without previous DM history were enrolled to study. Of 296 patients, 71 did not consent to evaluation, 27 patients were missing in follow-up investigation, 116 patients were critically ill that some were hemodynamically unstable or had acute myocardial infarction or severe sepsis, severe trauma or had psychiatric illness. Ultimately, 82 eligible patients were included the study (Fig. 1). The chief complaints of patients were gastrointestinal symptoms, neurologic symptoms, cardiopulmonary symptoms, etc (Table 1).

Among 82 eligible patients, 34 patients (41.4%) were newly diagnosed as DM. 38 patients presented presumptive symptoms of diabetes such as polyuria, polydipsia, polyphagia and current weight loss while 44 patients had none of those symptoms. Those with presumptive diabetes symptoms, 23 patients (60.5%) were diagnosed to diabetes other 15 patients (39.5%) did not. On the other hand, among the patients without any symptom of diabetes, 11 patients (25.0%) were diagnosed to diabetes while 33 patients (75.0%) weren’t. The difference between two groups was significant ($p=0.001$).

Regarding gender portion between the two groups,
those which include the patients who participated until the end of the study, male proportion in a group that had DM symptoms were 25 cases (65.8%), while non-symptomatic group was 24 (54.5%). The average age in group with symptoms was 54.3 years (CI, 47.8-60.8), and those in group without symptoms was 57.8 (CI, 52.9-62.8). The differences of basic characteristics between 2 groups were not statistically significant (Table 2).

The median random serum glucose level in a group with DM symptoms was 254.0 mg/dL (IQR, 220.5-372.0) and in the group without symptom was 232.0 (IQR, 213.0-287.75), the difference did not show statistical significance (p=0.143). However, HbA1c level in group with DM symptoms was relatively higher while the other group checked (7.5 (IQR, 5.7-9.9) vs 6.0 (IQR, 5.5-7.1), p=0.001) and numbers of newly diagnosed DM was high as well (p<0.001).

Overall, despite random serum glucose and HbA1c levels in the patients were correlated considerably (r=0.60, p<0.001), the relations between random serum glucose levels and diagnosis of DM were relatively low (Fig. 2).

**Table 1. Chief complaints of patients with random serum glucose ≥ 200 mg/dL.**

<table>
<thead>
<tr>
<th>Chief complaints</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal symptoms</td>
<td>27 (32.9)</td>
</tr>
<tr>
<td>Neurologic symptoms</td>
<td>17 (20.7)</td>
</tr>
<tr>
<td>Cardiorespiratory symptoms</td>
<td>13 (15.9)</td>
</tr>
<tr>
<td>Musculoskeletal symptoms</td>
<td>5 (6.1)</td>
</tr>
<tr>
<td>Genitourinary symptoms</td>
<td>5 (6.1)</td>
</tr>
<tr>
<td>Fever, General weakness</td>
<td>9 (11.0)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>6 (7.3)</td>
</tr>
<tr>
<td>Total</td>
<td>82 (100.0)</td>
</tr>
</tbody>
</table>

**Table 2. Basic characteristics and comparison between groups by symptoms of DM.**

<table>
<thead>
<tr>
<th>Included patients (n=82)</th>
<th>Symptoms of DM (n=38)</th>
<th>No symptoms of DM (n=44)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male), n (95% CI)</td>
<td>25 (50.7-80.9)</td>
<td>24 (39.8-69.3)</td>
<td>0.301</td>
</tr>
<tr>
<td>Age, mean (95% CI)</td>
<td>54.3 (47.8-60.8)</td>
<td>57.8 (52.9-62.8)</td>
<td>0.373</td>
</tr>
<tr>
<td>Glucose, mean (IQR)</td>
<td>254.0 (220.5-372.0)</td>
<td>232.0 (213.0-287.75)</td>
<td>0.143</td>
</tr>
<tr>
<td>HbA1c, median (IQR)</td>
<td>7.5 (5.7-9.9)</td>
<td>6.0 (5.5-7.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Diagnosis of DM, n (95% CI)</td>
<td>23 (45.0-76.1)</td>
<td>11 (12.2-37.8)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

n: number, CI: confidence interval, IQR: interquartile range.

**Discussion**

The symptomatic patient with random glucose level greater than 200 mg/dL had higher proportion of undiagnosed diabetes in our study (60.5% vs 25.0%, p=0.001). Even if the diabetic symptoms is very ambiguous and subjective, and the serum glucose level is influenced by the various situations, it states that patients with elevated serum glucose level at once in ED have great likelihood of undiagnosed DM, and have to be recommended for further evaluation at the endocrinology OPD. This finding is able to make the emergency physicians concern the undiagnosed DM patient that they have passed.

Recent studies have focused the validity of HbA1c as a screening tool for undiagnosed diabetes in emergency department. Some of studies discussed prevalence of undiagnosed DM in unselected ED population using HbA1c test, other studies analyzed the relationship of serum glucose level and HbA1c levels among patients with no history of diabetes throughout nations. However, unlike these previous studies, we studied about the prevalence of undiagnosed diabetes in ED patients with opportunistically checked hyperglycemia, random serum glucose level above 200 mg/dL, in a pragmatic view, retrospectively.

According to our study, 41.4% of patients were newly diagnosed as DM which is higher compared to previous reports. Perhaps the relatively increased number of undiagnosed diabetes might be a matter of patient selection. While other studies included unselected patient who visited ED, we confined to the patients with random serum glucose level over 200 mg/dL and no prior diabetes in real clinical situations that physicians should decide.
In practice, the proportion of cases only with newly diagnosed diabetes patients who completed the ED diabetes protocol of other studies was similar to our results.

From our study, the 11 patients (13.4%) who had hyperglycemia (200 mg/dL serum glucose) without symptoms of diabetes were newly diagnosed with DM. However, 15 patients (18.3%) were not diagnosed with DM even though they had symptoms of diabetes as well as hyperglycemia. Regarding these results, using only serum glucose level and clinical symptoms of diabetes for screening undiagnosed DM might be insufficient for patients who visit ED. Therefore, we suggested other tests in order to increase specificity as well as sensitivity of screening undiagnosed DM. HbA1c level, which is widely suggested as an additional screening DM tool, for instance, could be the complement to that problem\(^5\). It has advantages over fasting plasma glucose level and 2-hour oral glucose tolerance test since it doesn’t need fasting preparation and long test time\(^{11,12}\). In these points of view, HbA1c level combined with serum glucose level might be plausible in order to screen DM for undiagnosed patients visiting ED.

In regards to the relation between random glucose serum glucose and HbA1c to diagnosis of DM, though some patients had random serum glucose greater than 200 mg/dL, they were not diagnosed as DM (Fig. 2). After reviewing the medical records of these cases, we found that the episodes of transient glucose elevation were due to the stress of illness, not undiagnosed diabetes. On the other hand, most of the patients with HbA1c above 6.5% in ED were diagnosed as DM. The aforementioned patients who had high random serum glucose levels without diabetes also showed normal range HbA1c in the final examination. HbA1c over 6.5% could be the significant criterion for DM diagnosis. We thought that HbA1c test performed in ED had a value of discriminating for incidental hyperglycemia, undiagnosed DM versus stress-induced hyperglycemia. Naturally, it might had intermediate area hard to decide like other laboratory tests zone, i.e. some patients with high HbA1c levels patients were not diagnosed DM and vice versa (Fig. 2). Accordingly, DM diagnosis from HbA1c level would require more or less careful observation in borderline value.

Our study had several limitations. First, we had relatively small eligible patients to enrolled patients, primarily due to exclusion criteria based on clinicians’ decision, refusal to additional HbA1c test and outpatient revisit. This could create some potential selection bias, and overestimate the true prevalence of undiagnosed DM. Second, this study was performed at a single emergency medical center and the populations who visit ED would be different between emergency centers, which might restrict the applicability and generalizability. Third, we reviewed the medical records of patients such as chief complaint, past medical history, endocrinologist’s consultation, whether new diabetes medicine prescribed and follow-up serum glucose and HbA1c test value, etc, retrospectively. Since the information was strictly limited, it could affect the numbers of new diagnosis of undiagnosed DM patients, which could lead to misled results. For that reasons, well-controlled prospective multicenter cohort study is required in the future.

**Fig. 2.** Correlation between HbA1c and random serum glucose level for DM diagnosis (White circle indicates the patients not diagnosed as DM and black box indicates the patients diagnosed as DM. Red vertical reference line shows HbA1c level of 6.5%, red horizontal reference line shows random serum glucose level of 200 mg/dL.)

The prevalence of undiagnosed DM patients in patients with random serum glucose level over 200 mg/dL in the emergency department was considerably high, especially in the diabetic symptomatic groups. The patients who showed hyperglycemia incidentally in ED might be suspected to have undiagnosed DM if they had diabetic symptoms. Although with some limitations,
HbA1c levels would be of an assistance to detect these patients in emergency department with random serum glucose test. Moreover, emergency physicians should pay attention to opportunistic hyperglycemia and actively screen for diabetes to prevent long-term complications.

REFERENCES