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Prevalence and Factors Associated with Impaired Fasting Glucose among HIV-infected Patients in Bangbo Hospital, Samut Prakan, Thailand

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Abstract Diabetes in HIV infection was found to be associated with myocardial infarction and stroke. Impaired fasting glucose (IFG) will progress to diabetes within a few years. Limited data are available on IFG status among HIV-infected patients. We aimed to identify prevalence and define factors associated with IFG among HIV-infected patients in a community hospital of Thailand. Medical record of HIV-infected patients attending the HIV clinic of Bangbo hospital, Samut Prakan, Thailand, between January and December 2014 were reviewed. IFG was defined as fasting plasma glucose level between 100 and 125 mg/dL. Logistic regression analysis was used to define the factors associated with IFG. A total of 287 patients were enrolled. The mean age was 42.8 (SD = 8.9) years and 54.7% of them were males. Of all, 93 patients (32.4%) had family history of diabetes. All patients had received antiretroviral therapy (ART); 67.9% were on nevirapine (NVP)-based, 24.0% were on efavirenz (EFV)-based, and 8.0% were on protease inhibitor (PI)-based regimens. The median duration of taking ART was 5 years, with interquartile range (IQR) of 2-8 years. The median CD4 cell count was 428 (IQR = 310-603) cells/mm^3. The prevalence of IFG was 27.9%. In multivariate analysis, only age (OR 1.06; 95% CI, 1.02-1.09; p=0.002) and EFV-based regimen (OR 3.26; 95% CI, 1.71-6.21; p<0.001) were the factors significantly associated with IFG. IFG is prevalent among HIV-infected patients in Thailand. Screening of this condition should be performed in these patients, particularly in those who are advanced age or taking EFV-based regimen.

Key words: **impaired fasting glucose, HIV-infected patients**

Introduction

The provision of effective combined antiretroviral therapy has been proved that decline morbidity and mortality rate in HIV-1 infected patients[1]. However, prolonged exposure to antiretroviral therapy (ART) is associated with several metabolic syndromes[2-4], including dyslipidemia, overt diabetes, and insulin resistance, that ultimately increase the risk of

cardiovascular disease[4-6]. Impaired fasting glucose (IFG), an intermediate state of hyperglycemia, in which glucose levels do not meet criteria for diabetes but are too high to be considered normal, will progress to diabetes within a few years[7]. Diabetes in HIV infection was found to be associated with myocardial infarction and stroke[5,8]. Many factors have been found to be associated with new-onset type 2 diabetes among HIV-infected patients including protease inhibitor (PI), nucleoside and nucleotide reverse-transcriptase inhibitors (NRTIs), hepatitis co-infection, and some traditional risk factors[9-12]. However, few studies have focused on IFG in HIV infected patients. Early screening and intervention of this condition may reduce overt diabetes and cardiovascular disease-related morbidities and mortalities in long-term care. We aimed to identify prevalence and define factors associated with IFG among HIV-infected patients in community hospital of Thailand.

Material and Methods

Patients

Medical records from all HIV-infected patients who attended HIV clinic from January, 2014 to December, 2014 at Bangbo hospital – a 120-bed community hospital in Samut Prakan Province, Thailand, were reviewed. Inclusion criteria were HIV-infected patients with (1) aged more than 18 years and (2) having fasting plasma glucose (FPG) levels and/or glycated hemoglobin (HbA1C) results. The records were excluded if the patients had (1) HbA1C level of more than 6.5%, (2) previous diagnosis of diabetes, or (3) medical treatment of diabetes. Impaired fasting glucose (IFG) was defined as FPG levels between 100 and 125 mg/dL[13]. Demographic, behavioral, clinical, history of HIV infection, treatment, and laboratory data were retrieved from medical records. This study was reviewed and approved the Institution Review Board (Protocol number 001/58).

Statistical analysis

Mean (±SD), median (inter-quartile range, IQR), and frequencies (percentage) were used to show the patients' characteristics. Study patients were categorized into 2 groups based on FPG status: IFG group and normal FPG group. The mean values of continuous variables with normal distribution between the 2 groups were compared by Student's t-test. Mann-Whitney U-test was used to compare the median values of continuous variables with non-normal distribution. Categorical variables were compared by the Chi-square test and Fisher's exact test as appropriate. Univariate analysis was used to define the factors associated with impaired fasting glucose. Variables with a p-value less than 0.1 in univariate analysis were included in the multiple logistic regression model. All statistical analyses were performed using SPSS software, Version 15.0 (SPSS). A p-value of less than 0.05 was considered statistically significant.

Results

Two hundred and eighty seven patients were enrolled, according to our protocol. The mean (SD) age was 42.8 (8.9) years and 54.7% were males. Of all, 93 (32.4%) patients had family history of diabetes. The mean (SD) body weight and body mass index (BMI) was 51.2 (11.4) kg and 21.4 (3.9), respectively. All patients had received ART; 67.9% were on nevirapine (NVP)-based, 24.0% were on efavirenz (EFV)-based, and 8.0% were on protease inhibitor (PI)-based regimen. The median (IQR) duration of

taking ART was 5 (2-8) years. The median (IQR) CD4 cell count was 428 (310-603) cells/mm^3. Twenty one (7.4%) of 287 patients had detectable HIV viral RNA in blood. Other baseline characteristics were summarized in Table 1. The prevalence of IFG was 27.9%.

Categorized into two groups, IFG was found in 80 patients and normal FPG level in 207 patients. Comparing the two groups, no statistically significant differences (p>0.05) were found in gender, smoking history, drinking history, CD4 cell count, and duration of taking ART. In univariate analysis, age (p=0.002), body weight (p=0.039), family history of diabetes (p=0.028), dyslipidemia (p=0.003), EFV-based regimen (p=0.001), and PI-based regimen (p=0.063) were the factors that had p-values < 0.10; and were considered to be candidates for the multivariate model. In multivariate analysis, only age (OR 1.06; 95% CI, 1.02-1.09; p=0.002) and EFV-based regimen (OR 3.26; 95% CI, 1.71-6.21; p<0.001) were significantly associated with impaired fasting glucose (Table 2).

Discussion

The results from this study demonstrated that prevalence of impaired fasting glucose (IFG) among HIV-infected patients in Bangbo hospital, community hospital in the central region of Thailand, was

Table 1 Baseline characteristics of 287 patients

Characteristics	All (n=287)	IFG group (n=80)	Normal FPG group (n=207)	p-value
Gender, number (%)				0.187
- Male	157 (54.7)	49 (61.2)	108 (52.2)	
- Female	130 (45.3)	31 (33.8)	99 (47.8)	
Age, years (SD)	42.8 (8.9)	45.5 (8.8)	41.8 (8.7)	0.001
Body weight, kg (SD)	51.2 (11.4)	59.4 (9.6)	56.3 (11.8)	0.037
BMI, kg/m^2 (SD)	21.4 (3.9)	22.0 (3.0)	21.2 (4.1)	0.072
BMI category, number (%)				0.110
- Underweight (<18.5)	31 (11.3)	10 (12.7)	21 (10.7)	
- Normal weight (18.5-25)	206 (74.9)	53 (67.1)	153 (78.1)	
- Overweight (>25)	38 (13.8)	16 (20.3)	22 (11.2)	
Family history of diabetes (%)	93 (32.4)	34 (42.5)	59 (28.5)	0.025
Occupation, number (%)				0.882
- Employee	250 (87.1)	72 (90.0)	178 (86.0)	
- Housewife	11 (3.8)	2 (2.5)	9 (4.3)	
- Business owner	17 (5.9)	4 (5.0)	13 (6.3)	
- Priest	2 (0.7)	0 (0.0)	2 (1.0)	
- Civil servant	5 (1.7)	1 (1.2)	4 (1.9)	
- Agriculture	2 (0.7)	1 (1.2)	1 (0.5)	

Table 1 Baseline characteristics of 287 patients (cont.)

Characteristics	All (n=287)	IFG group (n=80)	Normal FPG group (n=207)	p-value
Smoking history, number (%)				0.524
- Current	61 (21.5)	19 (23.8)	42 (20.6)	
- Ex-smoking	44 (15.3)	14 (17.5)	30 (14.5)	
- Never	179 (62.4)	47 (58.8)	132 (63.8)	
Drinking history, number (%)				0.696
- Current	58 (20.2)	16 (20.0)	42 (20.3)	
- Ex-drinking	51 (17.8)	15 (18.8)	36 (17.4)	
- Never	176 (61.3)	49 (61.2)	127 (61.4)	
Duration of ART, years (IQR)	5 (2-8)	5 (2-7)	6 (2-8)	0.269
Nadir CD4 cell count, cell/mm^3 (IQR)	80 (17-193)	80 (16-193)	83 (18-193)	0.910
Current CD4, cell count, cell/mm^3 (IQR)	428 (310-603)	405 (291-566)	435 (312-630)	0.313
Detectable HIV viral load, number (%)	21 (7.4)	7 (8.8)	14 (6.9)	0.617
ART backbone, number (%)				0.350
- d4T+3TC	128 (46.7)	35 (43.8)	93 (44.9)	
- ZDV+3TC	115 (42.0)	39 (48.8)	89 (43.0)	
- TDF+3TC	31 (11.3)	12 (15.0)	32 (15.5)	
- TDF+ZDV	13 (4.5)	6 (7.5)	7 (3.4)	
ART regimens, number (%)				0.002
- NVP-based	195 (67.9)	42 (52.5)	153 (73.9)	
- EFV-based	69 (24.0)	29 (36.2)	40 (19.3)	
- PI-based	23 (8.0)	9 (11.2)	14 (6.8)	
Dyslipidemia, number (%)	112 (39.0)	43 (53.8)	69 (33.3)	0.002
Cholesterol, mg/dL (±SD)	196 (40.0)	199 (42.0)	195 (39.0)	0.354
HDL, mg/dL (±SD)	50.4 (13.6)	48 (14.0)	51 (13.0)	0.169
LDL, mg/dL (±SD)	116 (34.0)	156 (35.0)	115 (33.0)	0.844
Triglyceride, mg/dL (IQR)	123(84-186)	143 (99-224)	117 (78-179)	0.008

IFG - Impaired fasting glucose, FPG - fasting plasma glucose, BMI - body mass index, 3TC - lamivudine, ART - antiretroviral therapy, d4T - stavudine, EFV - efavirenz, NVP - nevirapine, PI - protease inhibitors, TDF - tenofovir, ZDV - zidovudine

27.9%. Age and ART with EFV-based regimen were significantly associated with IFG while PI-based regimen had a trend towards association.

The prevalence of IFG in our study was comparable to a study from Srivanich, et al[14], which was also conducted among Thai HIV-infected patients. Meanwhile, the prevalence of IFG in 2009 among Thai adults aged ≥ 20 years was only 10.6%[15]. Many

Table 2 Univariate and multivariate analyses of factors associated with impaired fasting glucose

Factors	Crude OR	p-value	Adjusted OR	p-value
Gender				
- Male	1.45 (0.86-2.45)	0.167		
- Female	1			
Age	1.05 (1.02-1.08)	0.002	1.06 (1.02-1.09)	0.002
Body weight	1.03 (1.01-1.05)	0.039	1.02 (0.99-1.05)	0.189
Body mass index	1.06 (0.97-1.14)	0.115		
Family history of diabetes	1.88 (1.07-3.32)	0.028	1.43 (0.80-2.55)	0.229
Smoking history				
- Current	1.35 (0.72-2.25)	0.355		
- Ex-smoking	1.35 (0.66-2.77)	0.413		
- Never	1			
Drinking history				
- Current	0.99 (0.51-1.93)	0.989		
- Ex-drinking	1.09 (0.55-2.16)	0.809		
- Never	1			
Duration of ART	0.95 (0.88-1.04)	0.276		
Nadir CD4 cell count	1.00 (0.99-1.01)	0.998		
Current CD4 cell count	0.99 (0.98-1.01)	0.297		
Detectable HIV viral load	1.37 (0.50-3.80)	0.546		
ART backbone				
- d4T+3TC	1			
- ZDV+3TC	1.01 (0.58-1.77)	0.977		
- TDF+3TC	0.62 (0.24-1.64)	0.334		
- TDF+ZDV	2.21 (0.70-7.04)	0.178		
ART regimens				
- NVP-based	1			
- EFV-based	2.73 (1.51-4.92)	0.001	3.26 (1.71-6.21)	<0.001
- PI-based	2.36 (0.95-5.82)	0.063	2.40 (0.92-6.27)	0.074
Dyslipidemia	2.30 (1.32-4.01)	0.003	1.56 (0.88-2.79)	0.131

ART - antiretroviral therapy, d4T - stavudine, 3TC - lamivudine, ZDV - zidovudine, TDF - tenofovir, NVP - nevirapine, EFV - efavirenz, PI - protease inhibitors

study reported the association of hyperglycemia or diabetes mellitus (DM) with protease inhibitors (PIs) use[16-18]. Moreover, nucleoside and nucleotide reverse-transcriptase inhibitors (NRTIs) were found to contribute to the disturbance of glucose metabolism[19,20]. These could be explained by the specific effect of PIs on the glucose transporter and of NRTIs on mitochondrial toxicity[19]. However, the effect of nonnucleoside reverse-transcriptase inhibitors (NNRTIs) on hyperglycemia or DM remains controversial. We found that EFV-based regimen was associated with impaired fasting glucose while Srivanich, et al[14] found NVP was a protective factor. A study from Manfredi, et al[21] showed that EFV had more impact on hyperglycemia than NVP. Nevertheless, the potential mechanism of the different dysglycemic patterns of these 2 NNRTI drugs was not well understood. We could not demonstrate association of PI-based regimen with IFG despite previous studies found association of hyperglycemia with PIs use[16-18]. This might be caused by inadequate number of subjects. Age was found to be a risk factor of IFG. This was consistent with age is the traditional risk factor of DM. For other traditional risks factor of DM in our study, however, we found no association with IFG. The explanation may be from small number of subjects or that we focused only on IFG, but not DM. Nonetheless, IFG correlates with DM which was found to be associated with myocardial infarction and stroke. IFG in HIV-infected patients seems to be more prevalent than that of non-HIV individuals. Screening of this condition should not be performed only patients who have traditional risk factors of DM, but also those who are taking EFV-based regimen.

There are several limitations of this study. First, selection bias might be occurred because we enrolled only patients who had FPG results. Second, because of the retrospective study design, a number of data on duration of HIV infection were missing. Timing of development of IFG could not be demonstrated either. Third, generalization may be limited because of single-centered study. Lastly, relatively small number of subjects may also limit our ability to detect significance of some factors.

In conclusions, IFG is common among HIV-infected patients in Thailand. Screening of this condition should be performed in these patients, particularly in those who are advanced age or taking EFV-based regimen. Large prospective studies are warranted to further evaluate the burden of IFG and DM in Thai HIV-infected patients.

Conflicts of interest

All authors declare that they have no conflict of interest.

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บทคัดย่อ: ความชุกและปัจจัยที่เกี่ยวข้องกับภาวะบกพร่องของน้ำตาลในเลือดหลังอดอาหารในผู้ป่วยติดเชื้อเอชไอวีที่ติดตามการรักษา ณ โรงพยาบาลบางบ่อ จังหวัดสมุทรปราการ

อนุวัตร ดิเรกสุนทร พ.บ.*; สุรศักดิ์ วิบูลชุติกุล พ.บ.**

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วารสารวิชาการสาธารณสุข 2558;24:1138-45.

ภาวะบกพร่องของน้ำตาลในเลือดหลังอดอาหารเป็นภาวะที่สามารถเปลี่ยนแปลงเป็นโรคเบาหวานในอนาคตได้ การศึกษานี้มีจุดประสงค์เพื่อหาความชุกและปัจจัยที่เกี่ยวข้องกับการเกิดภาวะนี้ในผู้ป่วยติดเชื้อเอชไอวีในโรงพยาบาลชุมชนในประเทศไทย ศึกษาวิจัยแบบย้อนหลัง โดยทบทวนเวชระเบียนผู้ป่วยติดเชื้อเอชไอวีที่มารักษาในคลินิกเอชไอวี โรงพยาบาลบางบ่อ จังหวัดสมุทรปราการ ระหว่างเดือนมกราคมถึงธันวาคม พ.ศ. 2557 และวิเคราะห์ความสัมพันธ์ระหว่างปัจจัยต่าง ๆและภาวะบกพร่องของน้ำตาลในเลือดหลังอดอาหารโดยใช้ logistic regression analysis ผู้ป่วยทั้งหมด 287 ราย มีอายุเฉลี่ย 42.8 ปี (SD = 8.9) เป็นชาย 54.7%, 93 ราย (32.4%) มีคนในครอบครัวเป็นโรคเบาหวาน ผู้ป่วยทั้งหมดได้รับยาต้านไวรัส ค่ามัธยฐานของระยะเวลาที่รับยาต้านไวรัสอยู่ที่ 5 ปี (interquartile range (IQR) = 2-8) ค่ามัธยฐานของปริมาณ CD4 เท่ากับ 428 (IQR = 310-603) cells/mm^3 พบความชุกของภาวะบกพร่องของน้ำตาลในเลือดหลังอดอาหารอยู่ที่ 27.9% และจาก multivariate analysis พบว่า อายุ (OR 1.06; 95%CI=1.02-1.09; p=0.002) และ efavirenz (EFV)-based regimen (OR 3.26; 95%CI=1.71-6.21; p<0.001) เป็นปัจจัยที่เกี่ยวข้องกับภาวะบกพร่องของน้ำตาลในเลือดหลังอดอาหารอย่างมีนัยสำคัญทางสถิติ ภาวะบกพร่องของน้ำตาลในเลือดหลังอดอาหารพบได้บ่อยในผู้ป่วยติดเชื้อเอชไอวี และควรมีการคัดกรองภาวะนี้โดยเฉพาะในผู้ป่วยที่อายุมากหรือได้ยาต้านไวรัสสูตรที่มี EFV

คำสำคัญ: **ภาวะบกพร่องของน้ำตาลในเลือดหลังอดอาหาร, ผู้ป่วยติดเชื้อเอชไอวี**