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BMI as a predictor of high fasting blood glucose among people living with HIV in the Asia-Pacific region

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Author Contributions

DK conducted data analysis and prepared the manuscript. DR and AJ provided guidance on analysis and critically reviewed the study and its content. All authors reviewed the results and manuscript, provided clinical expertise, and approved the final version of the paper.

Author Disclosure Statement

The authors have no conflict of interest to disclose.

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Abstract

Background: Non-Asian body mass index (BMI) classifications are commonly used as a risk factor for high fasting blood glucose (FBG). We investigated the incidence and factors associated with high FBG among people living with HIV (PLHIV) in the Asia-Pacific region, utilizing a WHO BMI classification specific to Asian populations.

Methods: PLHIV enrolled in a longitudinal cohort study from 2003 to 2019, receiving antiretroviral therapy (ART), and without prior tuberculosis (TB) were included. BMI at ART initiation was categorized using Asian BMI classifications: underweight (<18.5 kg/m^2), normal (18.5-22.9 kg/m^2), overweight (23-24.9 kg/m^2), obese (≥25 kg/m^2). High FBG was defined as a single post-ART fasting plasma glucose measurement ≥126mg/dl. Factors associated with high FBG were analyzed using Cox regression models stratified by site.

Results: A total of 3939 PLHIV (63% male) were included. Fifty percent had a BMI in the normal weight range, 23% were underweight, 13% were overweight, and 14% were obese; median age at ART initiation was 34 years (interquartile range [IQR] 29-41). Overall, 8% had a high FBG, with incidence rate of 1.14 per 100 person-years. Factors associated with increased hazard of high FBG included being obese (≥25 kg/m^2) compared to normal weight (HR=1.79, 95%CI: 1.31-2.44, p<0.001), and older age compared to those aged ≤30 years (31-40 years: HR=1.47, 95%CI: 1.08-2.01; 41-50 years: HR=2.03, 95%CI: 1.42-2.90; ≥51 years: HR=3.19, 95%CI: 2.17-4.69, p<0.001).

Conclusion: PLHIV with BMI above 25 kg/m^2 were at increased risk of high FBG. This indicates that regular assessments should be performed in those with high BMI, irrespective of classification used.

Keywords

Asia-Pacific; BMI; high fasting blood glucose; HIV

Background:

There is an increasing global burden of high fasting blood glucose (FBG), a precursor to diabetes mellitus (DM)(1,2). It has been estimated that the number of people with high FBG will double between 2000 and 2030, with greater numbers coming from low- and middle-income countries(3). While the use of combination antiretroviral therapy (ART) has increased survival among people living with HIV (PLHIV) by bringing HIV under control(4), this is being paralleled by the increasing burden of non-communicable diseases (NCDs)(5).

It has been shown that NCDs, including DM, are more common and start at younger ages among PLHIV on ART than in populations who are not living with HIV(6). It also has been found that the prevalence of high FBG is higher among PLHIV compared to the general population(5,7). Traditional risk factors of high FBG among PLHIV are obesity, male sex, older age, family history of diabetes, central obesity, race/ethnicity, dyslipidemia, and high blood pressure. Other potential risk factors include co-infections such as tuberculosis (TB) and hepatitis C virus (HCV), inflammation associated with the HIV virus itself, ART side effects (e.g. lipodystrophy, lipoatrophy), and low CD4 cell count(5,7–9).

Being overweight or obese based on body mass index (BMI) has been associated with high FBG among PLHIV across different regions(9–11). However, most of these studies have been conducted in African, American, and Western European countries using the international classification of BMI(11). The performance of BMI in predicting health outcomes has been debated for Asian populations, as there are concerns that the international classification underestimates those who are overweight or obese, and less accurately reflects fat percent relationships(12–15). Specifically, Asian populations tend to be at risk for NCDs at lower BMI by this classification(15–17). As a result, the WHO has developed an Asian classification system with modified BMI categories that may be more reliable(15).

This study seeks to understand the incidence rate of high FBG and its risk factors using BMI classifications for the Asian population. We investigate pre-ART BMI as a factor associated with high FBG among PLHIV in the Asia-Pacific region using the TREAT Asia HIV Observational Database (TAHOD) of the International epidemiology Databases to Evaluate AIDS (IeDEA) Asia-Pacific cohort.

Methods

Data source

This study analyzed longitudinal data of PLHIV enrolled in TAHOD which is a collaborative observational cohort with over 9600 PLHIV aged 18 years and older from 21 sites across 12 countries in the Asia-Pacific region. The TAHOD does not mandate regular visit schedule and all tests/interventions are performed according to the site's local practices. Detailed methods of this longitudinal cohort study have been published elsewhere(18). Institutional Review Board approvals were obtained at all participating sites, the data management and biostatistical center at the Kirby Institute (The University of New

South Wales Human Research Ethics Committee), and the coordinating center at TREAT Asia/amfAR.

Study population

Adult PLHIV enrolled in TAHOD from 2003 to September 2019 who had initiated ART were included in this analysis. The relationship between high FBG or DM and TB is well documented(19). There is also strong evidences of the relationship between active TB and low BMI(20). Therefore, PLHIV with prior history of TB were excluded from the analysis. To observe the effect of BMI on high FBG, PLHIV needs to have a pre-ART BMI measurement, defined as the closest BMI measurement 6 months prior to starting ART. Hence, PLHIV without pre-ART BMI measurement were also excluded from the analysis.

Statistical Methods

Our outcome of interest was high FBG, which was defined as having a single fasting plasma glucose measurement ≥126 mg/dL(21). Pre-ART BMI was calculated as the patient's pre-ART weight in kilograms divided by their height in metres squared. BMI was then categorized according to the WHO classification for Asian populations: underweight (<18.5 kg/m^2), normal weight (18.5-22.9 kg/m^2), overweight (23-24.9 kg/m^2), and obese (≥25 kg/m^2)(14,15,17).

Patient follow-up time began at ART initiation or cohort entry for those who initiated ART prior to cohort entry. Follow-up ended at the first occurrence of high FBG, or censored at transfer, death, loss to follow-up (LTFU) or the last follow-up visit. LTFU was defined as not having been seen in the clinic for more than 12 months after the last visit date without evidence of transfer.

Time-fixed covariates at the start of follow-up included pre-ART BMI, age, sex, mode of HIV exposure, history of AIDS-defining illness, CD4 cell counts, HIV RNA viral load, and initial ART regimen. Hepatitis B and hepatitis C co-infection status were also time-fixed covariates defined at the time when the PLHIV got tested positive for hepatitis B or C antibody respectively during follow-up period. Smoking status (ever/current smoking) and alcohol consumption status (ever/currently drinking above moderate or low risk consumption) were fixed at the most recent assessed date during follow-up. Year of ART initiation was included as time-fixed variable. Time-dependant covariates were high blood pressure, hyperlipidemia, smoking and alcohol drinking status.

High blood pressure was defined as having at least one measurement of systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg(22). Hyperlipidemia was defined as having a single result of fasting total cholesterol >200 mg/dL or fasting triglycerides >150 mg/dL(23). PLHIV were considered to have hepatitis B or hepatitis C co-infection if they ever tested positive for hepatitis B surface antigen or hepatitis C antibody, respectively. Consumption of ≤4 drinks/day or 14 drinks/week for males and ≤3 drinks/day or 7 drinks/week for females, according to US National Institute on Alcohol Abuse and Alcoholism criteria, was determined as moderate- or low-risk consumption of alcohol(24).

A Cox proportional hazards model stratified by site was used to identify factors associated with high FBG. Time to high FBG was plotted using Kaplan-Meier (K-M) curves. To identify independent factors associated with high FBG, covariates with p-value <0.10 in the univariate analysis were considered in the multivariate model using a backward stepwise selection process. Covariates with a p-value <0.05 were considered statistically significant in the multivariate model.

A sensitivity analysis was performed where PLHIV without FBG measurements and those with high FBG at start of follow-up were excluded from the study population.

Data management was performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA) and statistical analysis was performed using STATA SE software version 14.0 (Stata Corp., College Station, TX, USA).

Results

After excluding PLHIV with prior history of TB, there was a total of 7060 TAHOD PLHIV who initiated ART. Of those, there were 3121 PLHIV who did not have a pre-ART BMI available and were excluded. Of the 3939 PLHIV with available pre-ART BMI, the median follow-up time was 7.9 years (interquartile range [IQR] 4.0-10.3). Fifty percent had a pre-ART BMI in the normal weight range. The majority were male (63%) with heterosexual contact as the most common mode of HIV exposure (69%). At ART initiation, the median age was 34 years (IQR 29-41), the median CD4 cell count was 140 cells/μL (IQR 44-239), and the median viral load was 87,100 copies/mL (IQR 27,559-221,275). The majority of the PLHIV did not have a prior AIDS-defining illness (76%) and did not have high blood pressure (74%) (Table 1). The basic characteristics of PLHIV without pre-ART BMI measurements are described in the supplementary table (Supplementary table 1).

Among 3939 PLHIV included, 313 (8%) were identified as having high FBG during follow-up period. The crude incidence rate of high FBG was 1.14 per 100 person-years (/100pys) (Table 2).

Figure 1A is the K-M plot for time to high FBG by each pre-ART BMI category. At 5 years from ART initiation, the probability of not ever having reached FBG above the 126 mg/dL threshold was 96% for underweight BMI, 94% for normal weight BMI, 93% for overweight BMI, and 92% for obese BMI. Similarly, Figure 1B shows time to high FBG according to pre-ART age groups. At 5 years after ART initiation, the probability of not ever having reached FBG above the 126 mg/dL threshold was 96% for ≤30 years, 94% for 31-40 years, 93% for 41-50 years, and 88% for >50 years.

The univariate analysis suggested that BMI categories were associated with high FBG and other potential associated factors of high FBG were age group, gender, HIV mode of exposure, prior AIDS-defining illness, high blood pressure and hyperlipidaemia (Table 2).

In multivariate analysis, our study found being obese had an increased hazard of having high FBG compared to normal weight (HR=1.79, 95%CI: 1.31-2.44, p<0.001). Older age was associated with increased hazard of high FBG compared to those aged 30 or younger (age

group 31-40 years: HR=1.47, 95%CI: 1.08-2.01, p=0.014; 41-50 years: HR=2.03, 95%CI: 1.42-2.90, p<0.001; ≥51 years: HR=3.19, 95%CI: 2.17-4.69, p<0.001). PLHIV with prior AIDS-defining illness compared to those without (HR=1.34, 95%CI: 1.03-1.74, p=0.028) were found associated with increased hazard of high FBG. High lipid level compared to those with normal lipid level (HR=1.67, 95% CI: 1.27-2.20, p<0.001) were also associated with increased hazard of high FBG (Table 2).

Sensitivity analysis results

When we restricted our study population to PLHIV who were on combined ART, without prior history of TB, had pre-ART BMI, and pre-ART FBG measurements available, and excluded those who had high FBG at the ART initiation, there were 1517 PLHIV available to be included in the sensitivity analysis. Fifty percent had an Asian classification of BMI in the normal weight range. The PLHIV were largely male (64%). At ART initiation, the median age was 34 years ((IQR 29-41), the median CD4 cell count was 145 cells/μL (IQR 48-233), and the median viral load was 79,400 copies/mL (IQR 23,830-206,788). Majority of the PLHIV did not have a prior AIDS-defining illness (76%) and did not have high blood pressure at the time of ART initiation (74%). Heterosexual contact was the most common mode of HIV exposure (68%) (Supplementary table 2).

From this population, 171 (11%) were identified as having high FBG, giving an incidence rate of 1.62/100pys. Significant risk factors associated with high FBG in multivariate model included older age compared to those aged 30 or younger (age group 31-40 years: HR=1.55, 95%CI: 1.02-2.36; 41-50 years: HR=2.24, 95%CI: 1.40-3.60; ≥51 years: HR=3.09, 95%CI: 1.77-5.39, p<0.001) and hyperlipidemia compared to PLHIV with normal lipid level (HR=1.69, 95% CI: 1.17-2.42, p=0.005). Being female was associated with decreased hazard of high FBG compared to male (HR=0.61, 95%CI: 0.42-0.89, p=0.011) (Supplementary table 3). In both the main and sensitivity analysis, there was a reduction in hazard for high FBG in females compared to males. However, the association did not reach statistical significance in the main analysis, possibly due to a higher number of variables being included in the multivariate model.

BMI was not found to be associated with high FBG in the sensitivity analysis. In the univariate sensitivity analysis, the effects of different BMI categories compared to normal weight range were: underweight: HR=0.97, 95%CI: 0.66-1.43, p-value=0.89; overweight: HR=1.19, 95%CI: 0.72-1.96, p-value=0.50; and obese: HR=1.77, 95%CI:1.14-2.74, p-value=0.01, global p-value=0.06 (Supplementary table 3). When included in the multivariate model, there was no association between BMI and high FBG (global p-value =0.23). However, compared to normal weight range, the effects of different BMI groupings were: underweight: HR=0.97, 95%CI: 0.66-1.43, p-value=0.89; overweight: HR=0.99, 95%CI: 0.59-1.65, p-value=0.96; and obese: HR=1.55, 95%CI:1.00-2.42, p-value=0.05. This suggests that there was an underlying association between obese BMI and high FBG in the sensitivity analysis, however this association was borderline significant). For prior-AIDS defining illness, there was an increased hazard for FBG among those with a prior AIDS illness when the variable was included in the multivariate sensitivity analysis, however it did not reach statistical significance (HR=1.25, 95%IC: 0.87-1.81, p=0.23).

Discussion

In our cohort study of Asian PLHIV, we found that 8% ever had a high FBG test while on ART, with an incidence rate of 1.14/100pys. Being obese according to Asian BMI classifications, older age, having a prior AIDS-defining illness, and hyperlipidaemia were risk factors for high FBG. The study highlighted that being obese under the Asian classification of BMI was associated with high FBG.

The incidence rate of high FBG found in this study was similar to the incidence rate of DM among PLHIV in other Asian contexts. A retrospective analysis of 199,707 PLHIV in the Thai National AIDS Program had an incidence rate of 1.10 cases/100pys(25). In 2019, a study among adult PLHIV in the Asia-Pacific region exploring the incidence of new-onset DM after ART initiation using TAHOD dataset found the incidence rate of 1.08 cases/100pys(9). In contrast, our incidence rate is lower than those reported in studies conducted among PLHIV in other regions. The incidence of DM among adult PLHIV who participated in the Dominican HIV cohort was 2.80 cases/100pys(26). Interestingly, the results from the Data Collection on Adverse events of Anti-HIV Drugs cohort (D:A:D) showed a much lower incidence rate of DM at 0.29/100pys in 2015(27) and 0.45/100pys in 2020(28). These variations in rates could be explained by differences in sample size, length of follow-up time, and demographic characteristics of PLHIV, particularly of race/ethnicity.

Our study observed a significant association between pre-ART BMI categorised according to the Asian classification and the hazard of high FBG. In our study, those who were obese had almost twice the hazard of high FBG compared to those in the normal BMI range. Compared to Caucasian individuals, Asians have been found to have different adipose contents and partitioning, particular predisposition to increased abdominal adiposity, higher subcutaneous adipose tissue at any given BMI, and greater predisposition to cardio-metabolic disease risk at any given adiposity measure(16). Therefore, the international classification derived from the Caucasian population – BMI for underweight (<18.5 kg/m^2), normal weight (18.5-25 kg/m^2), overweight (25-30 kg/m^2) and obese (>30 kg/m^2) – may not be applicable to all Asians, and it was suggested separate classification of BMI for underweight (<18.5 kg/m^2), normal weight (18.5-22.9 kg/m^2), overweight (23-24.9 kg/m^2) and obese (≥25 kg/m^2) categories for the Asian population(14,15,17). However, to the best of our knowledge, few studies have used the Asian classification of BMI to study the association between BMI and high FBG or DM, especially among Asian PLHIV. A study among Thai adult PLHIV who participated in the HIV-NAT 006 cohort found that having pre-ART BMI ≥25 kg/m^2 was associated with over 2.5 times the hazard for new onset of DM compared to those who had BMI <25 kg/m^2 (29). Interestingly, international classifications of BMI were commonly used. A study assessing the incidence and associated factors of DM among PLHIV in Zimbabwe indicated that obesity (BMI ≥30 kg/m^2) had approximately 2.5 times the hazard for T2DM compared to those who have BMI <30 kg/m^2 (30). An analysis of retrospective data of PLHIV attending the 1917 Clinic at University of Alabama at Birmingham, USA, reported that obese PLHIV (BMI ≥30 kg/m^2) had approximately 3 folds increased hazard for T2DM compared to those who have BMI <25 kg/m^2 (31). The findings from our study, where those with BMI ≥25 kg/m^2 (obese in the Asian classification, and overweight in the international classification) were at increased risk

of having high FBG, suggest that irrespective of which BMI classification was used, it is important to monitor PLHIV whose BMI are elevated.

Age, one of the classical risk factors of high FBG, was found in this study to be associated with high FBG. This confirmed previous findings that the risk of high FBG among PLHIV increased with age(5,8,9,29). Association between age and high FBG has been reported in many studies, included an analysis among Thai PLHIV which indicated that being older than 35 years at ART initiation was associated with over 1.5 times the hazard for diabetes compared to the younger age group of less than 35 years(29). Findings from other regions also reported similar association. A large adult PLHIV Cohort in Jos, Nigeria also reported that PLHIV aged >40 years of age were 3.5 times more likely of having T2DM compared to those aged 40 or younger(32). Supporting this finding, an analysis on data from PLHIV aged 50 years and older in Vancouver, British Columbia also revealed a higher incidence rate of DM (1.61/100pys)(33). This highlights the significance of having blood glucose level checked as PLHIV age. In addition, efforts should be made to raise awareness around preventing or delaying the occurrence of high FBG among PLHIV, including maintaining a healthy diet and exercise regimen to control weight gain.

Those with prior AIDS-defining illness were found to be significantly associated with high FBG. The relationship between high FBG or DM and TB is well documented. A systematic review and meta-analyses of 44 published literatures indicated a strong positive association between DM and TB. All included studies were adjusted for at least age or sex, and estimates from majority of studies were also adjusted for different demographic characteristics such as socio-economic status, education, number of individuals in household, place of residence, and other potential confounders. In that review, diabetic PLHIV had been found to have between 2 to 4 folds increased risk of active TB compared to non-DM PLHIV(19). Due to the fact of this relationship, we excluded PLHIV with prior TB illness, but those with other AIDS-related conditions such as *Pneumocystic jirovecii pneumonia* (PCP) were still included. It is possible for medication such as steroids used to treat these existing illnesses to have an effect on FBG levels inducing hyperglycemia(34). For example, the use of steroid medications such as Prednisone or IV Methylprednisolone to treat PCP were known to increase FBG levels which could explain the association of prior AIDS and high FBG observed in our study.

Hyperlipidemia was also associated with high FBG among PLHIV in our cohort. This is consistent with a previous German study which showed that. high blood lipid level was more severe in PLHIV with high blood glucose level(35). Another study found that insulin resistance and risk of diabetes were related to high plasma triglyceride levels, but not at ART initiation(36). This two-way relationship indicated that the association between high FBG and hyperlipidemia is complex. Our findings suggest more attention should be given to monitor and control lipid and glucose levels in PLHIV, so that intervention can be done early to decrease the risk of these NCDs burden.

In our sensitivity analysis, risk factors associated with high FBG were older age, being male, and having hyperlipidemia. Although BMI did not reach statistical significance in the multivariate model, the effect of BMI ≥25 kg/m^2 was borderlineline significant when

included in the multivariate model which reflects the well-known underlying relationship with FBG, consistent with other studies (29,30,37,38).

There are multiple limitations to our study. There are limited data linkages between HIV clinics and different healthcare facilities. This means we might not have captured all of the cases who sought care at other private clinics or hospitals, so we might have outcome misclassification which could lead to underestimation of our incidence rate. Another limitation is the definition of high FBG used in our analysis. We utilized a single measurement of FBG as FBG was not measured frequently in our cohort. This could therefore lead to an over estimation of high FBG rates in our study. As our cohort did not collect glucose lowering drugs or data on other DM diagnostic tools, we were only able to define high FBG based on FBG measurements only.

Lastly, we were not able to adjust for unobserved confounders due to the nature of the observational cohort. As such, our results cannot be generalised to the wider PLHIV population.

Conclusion

Being obese in Asian BMI classification (overweight in the non-Asian classification), older age, having prior AIDS-defining illness, and hyperlipidemia were risk factors for high FBG. This suggests that the effects of BMI are equivalent to that of being above the healthy weight range in the non-Asian classification. Therefore, it is important to monitor PLHIV with high BMI, regardless of the classification used. Our study also highlights the importance of monitoring and routine screening for blood glucose level as PLHIV age. Few additional routine measures such as monitoring for BMI, regular screening of blood lipid levels before and after ART initiation may assist to reduce the burden of high FBG among PLHIV in the Asia-Pacific region.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Availability Statement

The data that supports the findings of this study are available from the corresponding author upon reasonable request.

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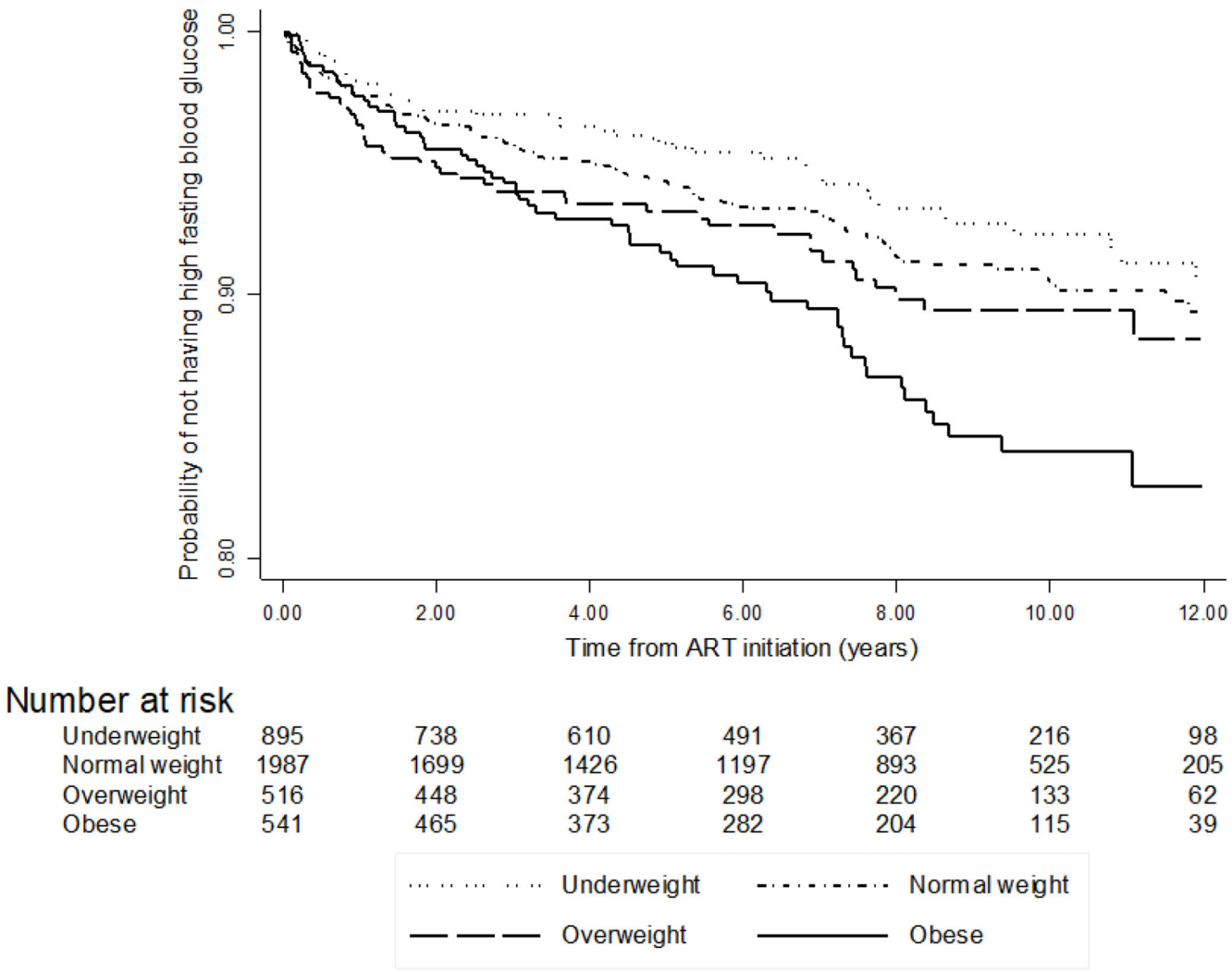

Figure 1A:
Kalpan–Meier curves of PLHIV by Asian BMI classification

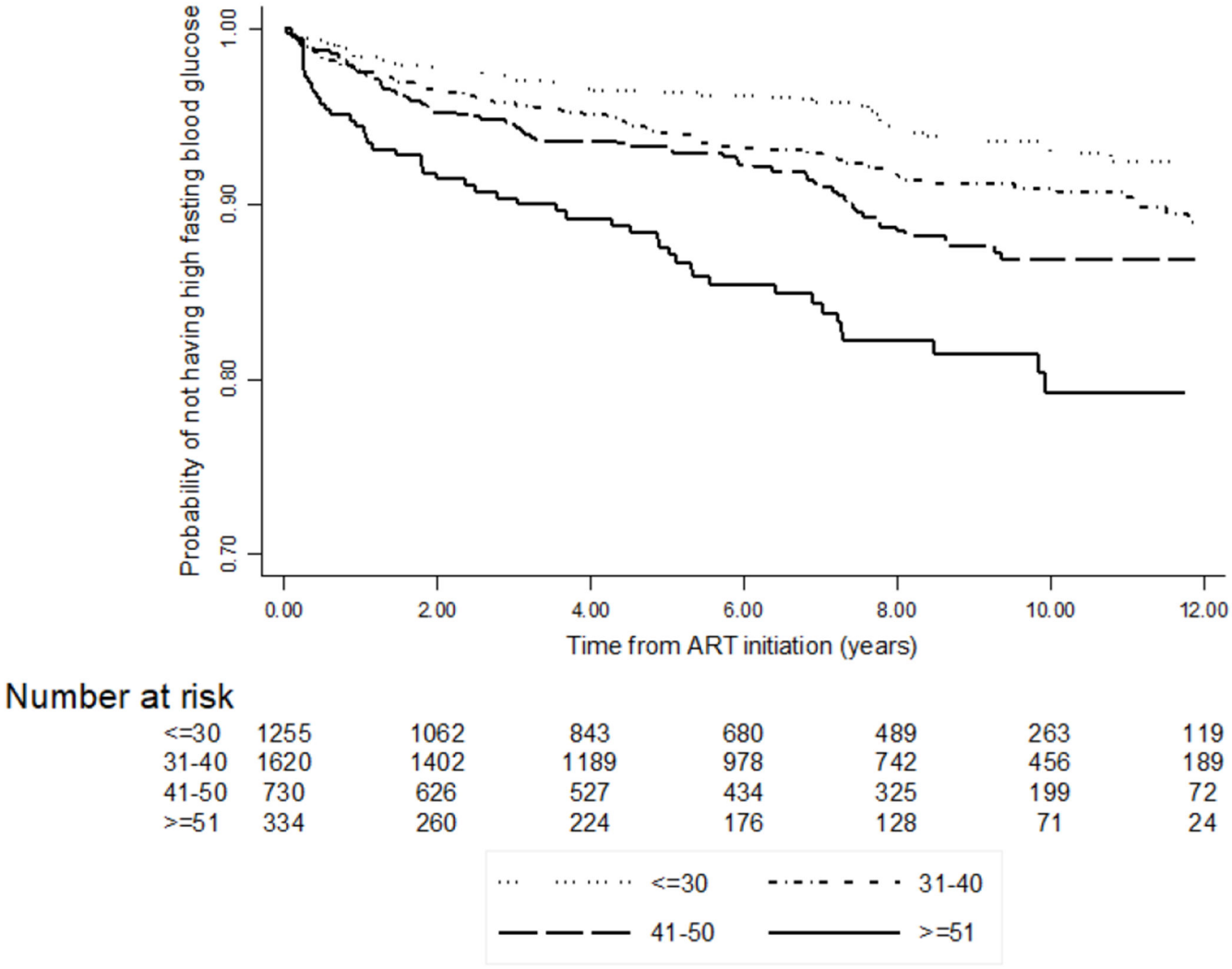

Figure 1B:
Kalpan–Meier curves of PLHIV by age group

Table 1.

Characteristics of PLHIV at ART initiation among those with available BMI and those with high FBG in TAHOD

Variables	Total PLHIV (%)	No. of PLHIV with high FBG (%)
Total	3939 (100)	313 (100)
Pre-ART BMI (Kg/m^2)		
Underweight (<18.5)	895 (23)	53 (17)
Normal weight (18.5-22.9)	1987 (50)	152 (49)
Overweight (23-24.9)	516 (13)	47 (15)
Obese (≥25)	541 (14)	61 (19)
Sex		
Male	2483 (63)	235 (75)
Female	1456 (37)	78 (25)
Age (years) at ART initiation		
Median (IQR)	34 (29-41)	37 (32-46)
≤30	1255 (32)	62 (20)
31-40	1620 (41)	126 (40)
41-50	730 (19)	73 (23)
≥51	334 (8)	52 (17)
HIV Exposure		
Heterosexual contact	2731 (69)	218 (70)
MSM	741 (19)	45 (14)
Injecting drug use	249 (6)	25 (8)
Other/Unknown	218 (6)	25 (8)
Prior AIDS		
No	3010 (76)	221 (71)
Yes	929 (24)	92 (29)
CD4 cell count (cells/μL) at ART initiation		
Median (IQR)	140 (44-239)	117 (31-205)
≤200	2459 (62)	221 (71)
210-350	966 (26)	66 (21)
351-500	216 (5)	10 (3)
≥501	113 (3)	5 (2)
Not reported	185 (5)	11 (3)
Viral load (copies/mL) at ART initiation		
Median (IQR)	87100 (27559-221275)	123800 (35536-329000)
≤100,000	1119 (28)	69 (22)
>100,000	933 (24)	84 (27)
Not reported	1887 (48)	160 (51)
ART regimen at ART initiation		
NRTI+NNRTI	3560 (90)	287 (92)
NRTI+PI	305 (8)	24 (8)

Variables	Total PLHIV (%)	No. of PLHIV with high FBG (%)
Other combination	74 (2)	2 (1)
High blood pressure at ART initiation		
No	2914 (74)	190 (61)
Yes	105 (3)	10 (3)
Not reported	920 (23)	113 (36)
Hyperlipidemia at ART initiation		
No	811 (21)	81 (26)
Yes	477 (12)	76 (24)
Not reported	2651 (67)	156 (50)
HBV surface antigen		
Negative	3042 (77)	268 (86)
Positive	352 (9)	33 (11)
Not reported	545 (14)	12 (4)
HCV antibody		
Negative	2723 (69)	254 (81)
Positive	424 (11)	48 (15)
Not reported	792 (20)	11 (4)
Smoking status (Ever smoked) at ART initiation		
Yes	1268 (32)	134 (43)
No	1062 (27)	63 (20)
Not reported	1609 (41)	116 (37)
Alcohol drinking status (Ever drunk) at ART initiation		
Yes	384 (10)	25 (8)
No	1261 (32)	48 (15)
Not reported	2294 (58)	240 (77)
Year of ART initiation		
≤2010	2552 (72)	264 (84)
2011-2013	749 (19)	42 (14)
2014-2019	338 (9)	7 (2)

TAHOD, TREAT Asia HIV Observational Database; No., number; FBG, fasting blood glucose; BMI, body mass index; AIDS, Acquired Immune Deficiency Syndrome; ART, anti-retro viral therapy; IQR, interquartile range; MSM, Men who have sex with men; HBV, hepatitis B virus; HCV, hepatitis C virus; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor

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Table 2.

Factors associated with High FBG - Cox model

					Univariate			Multivariate		
	No. PLHIV (%)	**Follow up (years)**	**High FBG events**	**Incidence rate (/100pys)**	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Total	3939 (100)	27499	313	1.14						
Pre-ART BMI (kg/m^2)							<0.001			<0.001
Underweight (<18.5)	895 (23)	6084	53	0.87	0.77	(0.56, 1.06)		0.77	(0.56, 1.05)	
Normal Range (18.5-22.9)	1987 (50)	14193	152	1.07	1			1		
Overweight (23-24.9)	516 (13)	3664	47	1.28	1.39	**(1.00, 1.94)**		1.23	(0.88, 1.71)	
Obese (≥25)	541 (14)	3558	61	1.71	1.95	**(1.43, 2.65)**		1.79	**(1.31, 2.44)**	
Sex										
Male	2483 (63)	17091	235	1.38	1					
Female	1456 (37)	10408	78	0.75	0.70	**(0.54, 0.92)**	0.009			
Age (years) at ART initiation							<0.001			<0.001
≤30	1255 (32)	8341	62	0.74	1			1		
31-40	1620 (41)	11807	126	1.07	1.62	**(1.19, 2.21**		1.47	**(1.08, 2.01)**	
41-50	730 (19)	5221	73	1.40	2.38	**(1.67, 3.38)**		2.03	**(1.42, 2.90)**	
≥51	334 (8)	2130	52	2.44	3.68	**(2.52, 5.39)**		3.19	**(2.17, 4.69)**	
HIV mode of exposure							0.07			
Heterosexual exposure	2731 (69)	19595	218	1.11	1					
MSM	741 (19)	4920	45	0.91	0.62	**(0.43, 0.90)**				
Injecting drug use	249 (6)	1474	25	1.7	1.16	(0.74, 1.82)				
Other/Unknown	218 (6)	1510	25	1.66	0.84	(0.55. 1.29)				
Prior AIDS										
No	3010 (76)	20646	221	1.07	1			1		
Yes	929 (24)	6853	92	1.34	1.32	**(1.02, 1.70)**	0.03	1.34	**(1.03, 1.74)**	0.028
CD4 (cells/μL) at ART initiation							0.30			
≤200	2459 (62)	17809	221	1.24	1					
201-350	966 (25)	6754	66	0.98	0.83	(0.63, 1.10)				
351-500	216 (5)	1175	10	0.85	1.04	(0.54, 1.97)				
≥501	113 (3)	493	5	1.01	1.80	(0.73, 4.46)				

					Univariate			Multivariate		
	No. PLHIV (%)	**Follow up (years)**	**High FBG events**	**Incidence rate (/100pys)**	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Not reported	185 (5)	1268	11	0.87						
Viral Load (copies/mL) at ART initiation							0.29			
≤100,000	1119 (28)	8062	69	0.86	1					
>100,000	933 (24)	13206	84	1.20	1.19	(0.86, 1.65)				
Not reported	1887 (48)	12420	160	1.29						
ART regimen							0.66			
NRTI+NNRTI	3670 (90)	24424	287	1.18	0.83	(0.54, 1.29)				
NRTI+PI	305 (8)	2613	24	0.92	1					
Other combination	74 (2)	462	2	0.43	0.65	(0.15, 2.79)				
High blood pressure										
No	~	22119	177	0.8	1					
Yes	~	1557	20	1.28	1.59	**(0.98, 2.58)**	0.06			
Not reported	~	3823	116	3.03						
Hyperlipidemia										<0.001
No	~	10659	81	0.76	1			1		
Yes	~	8764	169	1.93	1.99	**(1.52, 2.60)**	<0.001	1.67	**(1.27, 2.20)**	
Not reported	~	8075	63	0.78						
HBV surface antigen										
Negative	3042 (77)	21559	268	1.24	1					
Positive	352 (9)	2585	33	1.28	1.23	(0.85, 1.77)	0.27			
Not reported	545 (14)	3356	12	0.36						
HCV antibody										
Negative	2723 (69)	19745	254	1.29	1					
Positive	424 (11)	2793	48	1.72	0.99	(0.70, 1.40)	0.97			
Not reported	792 (20)	4961	11	0.22						
Smoking status (Ever smoked)										
Yes	~	9657	58	0.6	1					
No	~	6715	30	0.45	0.69	(0.43, 1.08)	0.10			
Not reported	~	11127	225	2.02						
Alcohol drinking status (Ever high)										

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					Univariate			Multivariate		
	No. PLHIV (%)	**Follow up (years)**	**High FBG events**	**Incidence rate (/100pys)**	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Yes	~	2648	13	0.49	1					
No	~	10349	11	0.11	0.68	(0.27, 1.68)	0.40			
Not reported	~	14502	289	1.99						
Year on ART							0.52			
≤2010	2852 (72)	22419	264	1.18	1					
2011-2013	749 (19)	4052	42	1.04	0.86	(0.60, 1.24)				
2014-2019	338 (9)	1028	7	0.68	1.35	(0.61, 2.98)				

No., number; FBG, fasting blood glucose; HR, hazard ratio; CI, confidence interval; ART, anti-retro viral therapy; MSM, Men who have sex with men; HBV, hepatitis B virus; HCV, hepatitis C virus; BMI, body mass index; AIDS, Acquired Immune Deficiency Syndrome; NRTI, nucleoside reverse transcriptase inhibitor;

Bold values represent significant covariates in the final model.