Table 15f. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Insulin Resistance, Asymptomatic Hyperglycemia, Diabetes Mellitus (Last updated April 7, 2021; last reviewed April 7, 2021)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Insulin Resistance, Asymptomatic Hyperglycemia, Diabetes Mellitus (DM)[a]	ZDV, LPV/r, and possibly other PIs	**Onset:** • Weeks to months after beginning therapy **Presentation:** • Asymptomatic fasting hyperglycemia (which sometimes occurs in the setting of lipodystrophy), metabolic syndrome, or growth delay • Symptomatic DM (rare)	**Children:** • Insulin resistance, 6% to 12% (incidence is higher during puberty, 20% to 30%) • Impaired fasting fasting glucose (FPG), 0% to 7% • Impaired glucose tolerance, 3% to 4% • DM, 0.2 per 100 child-years	**Risk Factors for Type 2 DM:** • Lipo-dystrophy • Metabolic syndrome • Family history of DM • High BMI (obesity)	**Prevention:** • Lifestyle modification **Monitoring:** • Monitor for signs of DM, change in body habitus, and acanthosis nigricans. • Obtain RPG levels at initiation of ART, 3–6 months after ART initiation, and yearly thereafter. • In patients with an RPG ≥140 mg/dL, obtain FPG after an 8-hour fast and consider referring the patient to an endocrinologist.	Counsel patient on lifestyle modification (e.g., implementing a diet low in saturated fat, cholesterol, trans fat, and refined sugars; increasing physical activity; ceasing smoking). Recommend that the patient consult with a dietician. If the patient is receiving ZDV, switch to TAF, TDF, or ABC. **For Patients with Either an RPG ≥200 mg/dL Plus Symptoms of DM or an FPG ≥126 mg/dL:** • These patients meet diagnostic criteria for DM; consult an endocrinologist. **For Patients with an FPG of 100–125 mg/dL:** • Impaired FPG suggests insulin resistance; consult an endocrinologist. **For Patients with an FPG <100 mg/dL:** • This FPG is normal, but a normal FPG does not exclude insulin resistance. Recheck FPG in 6–12 months.

[a] Insulin resistance (IR), asymptomatic hyperglycemia, impaired fasting plasma glucose (IFPG), impaired glucose tolerance (IGT), and diabetes mellitus (DM) form a spectrum of increasing severity.

IR: Often defined as elevated insulin levels for the level of glucose observed.

IFPG: Often defined as an FPG of 100–125 mg/dL.

IGT: Often defined as an elevated 2-hour PG of 140–199 mg/dL in a 75-g OGTT (or, if the patient weighs <43 kg, 1.75 g per kg of glucose up to a maximum of 75 g).

DM: Often defined as either an FPG ≥126 mg/dL, an RPG ≥200 mg/dL in a patient with hyperglycemia symptoms, an HgbA1c of ≥6.5%, or a 2-hour PG ≥200 mg/dL in an OGTT.

However, the Panel does not recommend performing routine measurements of insulin levels, HgbA1c, or glucose tolerance without consulting an endocrinologist. These guidelines are instead based on the readily available RPG and FPG levels.

Key: ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; BMI = body mass index; FPG = fasting plasma glucose; HgbA1c = glycosylated hemoglobin; LPV/r = lopinavir/ritonavir; mg/dL = milligrams per deciliter; OGTT = oral glucose tolerance test; the Panel = Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV; PG = plasma glucose; PI = protease inhibitor; RPG = random plasma glucose; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

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