Table 15f. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Insulin Resistance, Asymptomatic Hyperglycemia, Diabetes Mellitus *(Last updated April 16, 2019; last reviewed April 16, 2019)*

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Associated ARVs</th>
<th>Onset/Clinical Manifestations</th>
<th>Estimated Frequency</th>
<th>Risk Factors</th>
<th>Prevention/Monitoring</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin Resistance, Asymptomatic Hyperglycemia, DM*</td>
<td>ZDV, LPV/r, and possibly other PIs</td>
<td>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)</td>
<td>Children: • Insulin resistance, 6% to 12% (incidence is higher during puberty, 20% to 30%) • Impaired fasting glucose, 0% to 7% • Impaired glucose tolerance, 3% to 4% • DM, 0.2 per 100 child-years</td>
<td>Risk Factors for Type 2 DM: • Lipodystrophy • Metabolic syndrome • Family history of DM • High BMI (obesity)</td>
<td>Prevention: • Lifestyle modification Monitoring: • Monitor for signs of DM, change in body habitus, and acanthosis nigricans. Obtain RPG Levels at: • Initiation of ARV therapy • 3 months–6 months after therapy initiation • Once a year thereafter For RPG ≥140 mg/dL: • Obtain FPG after an 8-hour fast and consider referring the patient to an endocrinologist.</td>
<td>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 patient is receiving ZDV, change to TAF, TDF, or ABC. For Either RPG ≥200 mg/dL Plus Symptoms of DM or FPG ≥126 mg/dL: • Patient meets diagnostic criteria for DM; consult an endocrinologist. FPG 100–125 mg/dL: • Impaired FPG suggests insulin resistance; consult endocrinologist. FPG &lt;100 mg/dL: • This FPG is normal, but a normal FPG does not exclude insulin resistance. Recheck FPG in 6 months–12 months.</td>
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</tbody>
</table>

* Insulin resistance, asymptomatic hyperglycemia, and DM form a spectrum of increasing severity.

**Insulin Resistance:** Often defined as elevated insulin levels for the level of glucose observed.

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

**Impaired Glucose Tolerance:** 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).

**Diabetes Mellitus:** Often defined as either an FPG ≥126 mg/dL, and RPG ≥200 mg/dL in a patient with hyperglycemia symptoms, an HgbA1c of ≥6.5%, or a 2-hour PG ≥200 mg/dL after 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 to Acronyms:** ABC = abacavir; ARV = antiretroviral; BMI = body mass index; dL = deciliter; DM = diabetes mellitus; FPG = fasting plasma glucose; HgbA1c = glycosylated hemoglobin; LPV/r = lopinavir/ritonavir; OGTT = oral glucose tolerance test; PG = plasma glucose; PI = protease inhibitor; RPG = random plasma glucose; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine
References


