## **Nonclassic WFS1 Spectrum Disorder (WFS1-SD)**

### **🔍 Suggestive Clinical Findings**

Nonclassic WFS1-SD should be considered in individuals with one or more of the following:

* **Diabetes mellitus** (usually diagnosed after age 16)
* **Optic atrophy** (typically later onset than in classic form)
* **Sensorineural hearing loss** (low-tone, may be profound and congenital)
* **Neonatal diabetes, congenital deafness, and/or cataracts**

📌 *Family history may suggest autosomal dominant inheritance, but sporadic (de novo) cases are also observed.*

### **🧬 Diagnosis**

* **Confirmed via molecular genetic testing**:
  + A **heterozygous** pathogenic (or likely pathogenic) variant in *WFS1*.

### **🧠 Clinical Description**

* **Rarer** and generally **milder** than classic WFS1-SD.
* **Most common phenotype**: Isolated **optic atrophy** and **congenital deafness**.
* Other observed combinations include:
  + **Diabetes + optic atrophy + deafness**
  + **Isolated adult-onset diabetes mellitus**
  + **Congenital cataracts (without other features)**
  + **Low-frequency progressive hearing loss** (DFNA6/14/38)
  + **Neonatal diabetes, deafness, and cataracts** (de novo mutations)

*Unlike classic WFS1-SD, nonclassic forms are not associated with progressive neurodegeneration. Brain MRI is typically normal.*

### **🧑‍⚕️ Management**

There is no cure — treatment is **supportive and symptom-specific**. A **multidisciplinary approach** is essential and may include:

* Endocrinology
* Audiology & cochlear implant services
* Ophthalmology & low vision aids
* Genetic counseling
* Social work and community support coordination

### **Surveillance Recommendations**

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| **System** | **Evaluation** | **Frequency** |
| **Diabetes mellitus** | HbA1c monitoring | Annually until diagnosed with insulin dependent diabetes mellitus; then as per standard care) |
| **Optic atrophy** | Full eye exam (visual acuity, color vision, fundoscopy, etc.) | Annually |
| **Hearing impairment** | Audiogram + speech discrimination testing | Annually |
| **Psychosocial support** | Social work, care coordination, equipment/supplies management | Ongoing as needed |
| **Genetic counseling** | For family planning or new diagnostic questions | As indicated |

### **👶 Inheritance & Genetic Counseling**

* **Autosomal dominant** inheritance (heterozygous variant in *WFS1*)
* Can be inherited or **de novo**
* **50% recurrence risk** if a parent is affected
* **1% recurrence risk** if neither parent has the variant (possible germline mosaicism)

**Based on the GeneReviews:**  https://www.ncbi.nlm.nih.gov/books/NBK4144/