Diabetes mellitus is a spectrum of conditions with a wide variation in clinical presentation but with the common feature of chronic hyperglycaemia. The inheritance of diabetes has been the subject of intensive investigation. In the past decade a number of gene mutants have been identified that represent high penetrance risk genes for diabetes. These so-called monogenic forms of diabetes comprise the various forms of maturity-onset diabetes of the young (MODY) [1] and mitochondrial diabetes [2]. Together, these monogenic forms account for less than 3% of the total number of diabetes cases.

A maternally inherited A to G 3243 mutation in the mitochondrial tRNA Leu gene (A3243G mtDNA mutation) was originally described in patients with the MELAS syndrome (mitochondrial encephalomyopathy, lactic acidosis and stroke like episodes). However, this mutation is also associated with several other phenotypes. In 1992, a subtype of diabetes called maternally inherited diabetes and deafness (MIDD) was reported to co-segregate with the same point mutation [2]. MIDD was initially characterized by a maternal history of diabetes, associated hearing loss, or both, without major neurological defects. In MIDD, diabetes seems to be due primarily to a defect in insulin secretion, while insulin sensitivity is unaltered [3]. In most reported series of MIDD, diabetes appears as a non-insulindependent form with a young age of onset and a normal or low BMI [4]. In clinical practice, these patients can be classified as having type 1 or type 2 diabetes depending on the severity of the insulinopenia. Many investigators had previously screened type 2 adult diabetic patients in Europe and Japan for the A3243G mtDNA mutation and had found this mutation in 0.5% to 3% of their patients, the highest prevalence being observed in the Japanese population [5-8]. However, the contribution of MIDD to the prevalence of type 1 diabetes has been less well investigated [9,10].

The aim of the present study was to establish the prevalence of A3243G mtDNA mutation in unselected adult patients previously diagnosed with type 1 diabetes.

One hundred and thirty-eight unrelated caucasian patients with type 1 diabetes entered in the Type 1 Diabetes Registry of Catalonia between 1st January 1987 and 31st December 1988 were screened for the A3243G mtDNA mutation ten years after onset. Type 1 diabetes was diagnosed based on the WHO criteria [11]. Clinical features of patients screened are displayed in table I. The A3243G mtDNA mutation was identified in peripheral blood mononuclear cells (PBMCs). PBMCs were isolated by Ficoll-Paque density gradient centrifugation and total

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**Key-words:** Diabetes mellitus · Mitochondrial diabetes · A3243G mtDNA mutation · Type 1 diabetes · Prevalence · Catalonia.


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**Mots-clés :** Diabète sucré · Diabète mitochondrial · Mutation A3243G de l’ADN mitochondrial · Diabète de type 1 · Prévalence · Catalogne.

Prévalence de la mutation A3243G de l’ADN mitochondrial chez des patients atteints de diabète de type 1 de l’adulte en Catalogne

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DNA was extracted by using a commercial kit (Epicentre Biotechnologies, Madison, Wisconsin). The A3243G mtDNA mutation was determined by restriction fragment length polymorphism (RFLP) as previously described [12]. The lower limit of detection is 3% of mitochondrial mutated DNA. Data were stored and analyzed using the software package SPSS 10 for Windows (SPSS, Inc, Chicago, IL). Mean value and standard deviation is presented for quantitative variables, while descriptive results are presented as proportions.

The A3243G mtDNA mutation was found in 1 out of 138 patients diagnosed with type 1 diabetes (prevalence 0.72%). The proband was a 30 year old man, who was diagnosed with type 1 diabetes at the age of 17. At the moment of the evaluation he showed bilateral neurosensory hearing loss. He had one sister also diagnosed with type 1 diabetes, but there was no maternal history of diabetes.

In agreement with previous studies in type 1 diabetic patients [9,10], we found a low prevalence of the A3243G mtDNA mutation among an unselected caucasian population of type 1 diabetic subjects. Moreover, it does not differ from the prevalence of this mutation in caucasian type 2 diabetic populations [6,8]. However, as blood was used to identify mtDNA mutations instead of other tissues such as buccal or urine cytology, it is possible that the prevalence of MIDD was underevaluated. Nevertheless, our results reinforce the concept that A3243G mtDNA mutation makes only a minor contribution to the pathogenesis of type 1 diabetes. Thus, like in previous studies, the screening of the A3243G mtDNA mutation among type 1 phenotype diabetic patients should be indicated only in patients who present other clinical features suggesting a mitochondrial alteration, such as maternal inheritance and neurosensory deafness.

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