High prevalence of a missense mutation of the glucokinase gene in gestational diabetic patients due to a founder-effect in a local population

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Abstract:

Summary A high proportion of the female patients who are members of maturity onset diabetes of the young (MODY) pedigrees, and whose diabetes mellitus is due to a glucokinase mutation, originally presented with gestational diabetes. To establish whether glucokinase mutations could be a common cause of gestational diabetes, we studied 50 subjects who presented with gestational diabetes and on follow-up had hyperglycaemia (5.5-10.0 mmol/l). Screening for glucokinase mutations using single-stranded conformational polymorphism (SSCP) analysis detected a missense mutation at position 299 (Gly299 M Arg) in three subjects. As two pedigrees in the Oxford area had the same glucokinase mutation, we suspected the role of a founder-effect, and carried out pedigree extension, haplotype construction (using microsatellite markers GCK1 and GCK2) and mutation screening of at-risk subjects from the same geographical area. One of the gestational diabetic subjects was found to be related to one of the previous pedigrees via her paternal grandmother. Subjects with the mutation were found to have the Z + 4/2 (GCK1/GCK2) haplotype, suggesting that the observed high prevalence of the Gly299 M Arg glucokinase mutation in the Oxford region was due to a founder-effect. Since glucokinase mutations predominantly induce subclinical hyperglycaemia, it is likely that in the locality of other pedigrees there will be undiagnosed subjects with the same glucokinase mutation, which remains undetected unless pregnancy occurs. [Diabetologia (1996) 39: 1325-1328]