COMMENTS AND RESPONSES

Comment on: Chakera et al. Antenatal Diagnosis of Fetal Genotype Determines if Maternal Hyperglycemia due to a Glucokinase Mutation Requires Treatment. Diabetes Care 2012;35:1832–1834

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We have read with great interest the article by Chakera et al. (1) describing two cases of gestational diabetes mellitus due to a mutation in the glucokinase (*GCK*) gene. As a result of antenatal genetic testing, the fetuses had inherited the *GCK* mutation. Neither fetuses nor mothers received insulin treatment for established maternal hyperglycemia in the third trimester, and the children had a normal birth weight and no metabolic complications. The data of Chakera et al. seemed to confirm our published theory; therefore, a nonmutated *GCK* child from a maturity-onset diabetes of the young type 2 (MODY2$^+$) mother may have the same complications as a diabetic mother's son and, in this case, it's very important to treat the mother (also with insulin if necessary) to prevent macrosomia and neonatal hypoglycemia—but the situation is different if both mother and child carry a genetic mutation predisposing to MODY2. In this case, the fetus has poor insulin secretion that, if not increased by exposure to high maternal glycemic levels, may result in inadequate intrauterine growth and the birth of a small-for-gestational-age (SGA) infant (2). The SGA infant has greater postnatal risks than the large-for-gestational-age infant: low birth weight for gestational age represents an independent risk factor for neonatal mortality and morbidity (3). So, in 2010 we formed a "South Italian Group of Study on Diabetes Pregnancy" that involves the University of Molise, the Second University of Naples, the C.E.I.N.G.E. (Advanced Biotechnology–University "Federico II" of Naples), several hospitals of south Italy, and several National Scientific Society members (A.O.G.O.I. and S.C.C.L.) to study monogenic diabetes in pregnancy. At present, we have screened 264 women with gestational diabetes mellitus for Hyperglycemia and Adverse Pregnancy Outcome study criteria, including four cases of MODY2 and one of MODY type 1. We have also estimated the possibility of using serial antenatal ultrasound to screen the children of women with MODY2, but we think that there is a great variability in calculating the fetal weight related to the formulae used, the experience of examiners, and the high possibility of an error (5–14%) in the estimated fetal weight (4,5); moreover, the possibility of other concomitant causes of fetal macrosomia may represent a further confusing factor for a correct diagnosis. Therefore, the serial antenatal ultrasound may be a promising method to screen the children of women with MODY2, but at present it is indispensable to establish the criteria for a correct exam, to characterize the cutoff (>75th or 90th centile?) for a correct diagnosis, and to evaluate the sensibility and the specificity of methods to detect the unaffected fetuses. At present, although chorionic villus sampling and amniocentesis are associated at the 1% miscarriage rates, they represent the gold standard for a genetic diagnosis of MODY in the fetus; but are we ready to perform the amniocentesis for every MODY2$^+$ mother? Is the risk of these procedures acceptable to diagnose a case of MODY? We are sure that an international debate can help us to develop new methods of investigation associated with a new vision, a new approach, and a new management of this disease.

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