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Letter to the Editor

Dizygotic Twins Concordant for Down Syndrome: Implication for Establishing a National Birth Defect Registry in Iran

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Dear Editor-in-Chief

The prevalence of Down Syndrome (DS) has increased in association with increasing maternal age (1). The prevalence of multiple births, particularly dizygotic births has also increased in association with increasing maternal age (2). Surprisingly, the risk of DS in twins is significantly lower than in singletons due to early fetal loss of DS in multiple pregnancies, particularly in pregnancies concordant for DS (2). Based on a large population-based study in Europe which studied 14.8 million birth, the prevalence of babies born as twins concordant for DS was 7.20 (95%CI 5.96-8.69) per million births, the majority of which were MZ twins (3). Dizygotic twins (DZ) concordant for DS are extremely rare and approximately 4 per 10 million births (3). There are some reports on DZ twins concordant for DS (4-7), but to the best of our knowledge, the first report from Iran.

We describe two intellectually disabled siblings referred to Genome Genetic Laboratory and Counseling Center (Tehran, Iran) in 2016. They were 19-yr-old dizygotic twins (zygosity inferred from unlike sex) who showed clinical features consistent with DS. The mother of twins was 35 yr old, at the time of pregnancy. She had two healthy pregnancies when she was 22 and 26. The parents of the twins were married by non-consanguineous marriage. No history of DS was discovered on inquiry into the family history. The possibility of parents carrying a Robert sonian translocation was rejected as trisomy 21 was confirmed by karyotyping each affected co-twin: Twenty metaphase cells were studied based on G-banding technique at the 450-500 bands resolution. All metaphase cells revealed an extra chromosome 21.

DZ twins concordant for DS are very rare. A 35-yr-old woman has a 1/270 risk of having one baby with DS. Therefore, a 35-yr-old woman's risk of having a DZ twin both with DS is calculated by multiplying 1/270 times 1/270 times the risk of DZ twinning. The risk of DZ twinning varies over time, geographic location and genetic disposition; however, the average risk is 13 times per 1000 pregnancies (8). Hence, in this case, the risk of having DZ twin both with DS is expected to be less than 2 per 10 million live births. Interestingly, the actual risk of DS in twins is substantially less than the risk routinely used in genetic counseling of twin gestations (3). A large population-based study in Europe suggests that at any age, a woman is 32% rather than 100% more likely to have at least one baby with DS in a DZ twin pair compared to singletons, suggesting that babies who are DZ twin with Down syndrome

are less likely to survive to diagnosis (3). Therefore, the data used in genetic counselling of singleton pregnancies do not apply to twin gestations and accurate data about the risk of DS in multiple pregnancies are required.

Birth defects (whether chromosomal or non-chromosomal) are common, costly and critical. Accurate risk estimate in genetic counselling for birth defects requires accurate statistics related to the prevalence of birth defects. Counselling accurate statistics are obtained through large population-based studies. Given that birth defects are multifactorial in nature, each nation should have their own statistics. Therefore, nation-wide registering of birth defects is necessary to gather reliable statistics. This information is essential for public health monitoring, health care provision and supporting birth defect research. In most developed countries, there are reliable statistics on the prevalence of birth defects obtained from population-based studies. Establishing birth defect registries (BDRs) are particularly essential in low resource or developing countries to plan care and prevention services at local and national levels (9). The data obtained from national BDR would be useful in providing statistics required for genetic counseling such as the prevalence of twins with DS and the rate of DZ twinning in Iran, or support research on genetic variants predisposing to chromosomal non-disjunction.

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