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Letter to the Editor

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Significance of Hardy-Weinberg Equilibrium in Case Control

Hemant Kumar Bid Rama D. Mittal

Department of Urology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

Dear Sir,

This is in reference to the paper 'Association of E-Cadherin Gene 3′-UTR C/T Polymorphism with Calcium Oxalate Stone Disease' by Tsai et al. (Urol Int 2003;70:278–281). The authors investigated the role of polymorphism and demonstrated the association of the E-cadherin gene with calcium oxalate stone disease. The article is interesting but there are some points which are not clear. We feel that the control population is not in genetic equilibrium. A simple rule is that the frequency of the heterozygous (CT) class cannot exceed 50%; however, the authors report a frequency of 88%. Applying their reported allelic frequencies to the Hardy-Weinberg calculation confirms that the genotype distribution in the control population is significantly different from the expected distribution and thus not in equilibrium. It may be, for instance, that different ethnic groups (with different allelic frequencies) do not inter-marry and equilibrium is not reached. A variety of other factors could also contribute to this non-equilibrium, such as large migrant populations. Hence to conclude the differences between the normal and the disease population cannot be addressed until this issue is resolved. If ethnicity is the source of the problem, such studies will have to be confined to single ethnic groups.

Rama D. Mittal, MD, Department of Urology
Sanjay Gandhi Post Graduate Institute of Medical Sciences
Lucknow, UP 226014 (India)
Tel. +91 522 2668 700/800/900 ext. 2126/2115
Fax +91 522 668 017, E-Mail rmittal@sgpgi.ac.in

Reply

Wen-Chi Chen[a, b] Fuu-Jen Tsai[b, c]

Departments of [a] Urology, [b] Medical Genetics, and [c] Pediatrics, China Medical University Hospital, Taichung, Taiwan

Dear Sir,

In response to the letter about our article 'Association of E-Cadherin Gene 3′-UTR C/T Polymorphism with Calcium Oxalate Stone Disease' [1], we make the following points regarding the Hardy-Weinberg equilibrium.

(1) The Hardy-Weinberg equilibrium principle is calculated for an autosomal recessive trait disease (when a mutant allele leads to a severe disorder in the homozygous state which is present in a population with an undetectable heterozygous state) [2]. Only homozygosity comes to attention as a result of illness. This principle is valid for a single gene disease [3]. Therefore, a simple formula presents as $(P + Q = 1)$ and can be applied to $(P^2 + 2pq + Q^2 = 1)$ to calculate the carrier frequencies and simple risk for counseling.

(2) We used genetic polymorphism to test the association of some genes with a commonly seen disorder. Instead of single gene disease, a multifactorial disease is studied. However, the nucleotide polymorphism is not strong enough to result in a disease.

Table 1. Distribution of E-cadherin gene 3′-UTR C/T polymorphism among the test populations

	CC	CT	TT	Total
Controls	5 (4.9%)	88 (85.4%)	10 (9.7%)	103
Controls from myoma group	0	73 (93.6%)	5 (6.4%)	78
Controls from endometriosis group	10 (6.7%)	123 (82%)	17 (11.3%)	150

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Therefore, this allele will not eventually disappear or reach a frequency equilibrium, i.e. a selective disadvantage for individuals will not occur.

(3) Ethnic difference does exit. The polymorphisms reported in the literature from Caucasians, such as TGF-β1 (–800), THSR (D36H), and collagen-related gene (COL3A1 gene exon 32 and COL1A1 intron 1), were not found in our laboratory. But we did find that the frequency of CT heterozygotes of the E-cadherin gene 3′-UTR polymorphism in different study groups (table 1) was the same as our data [1]. Therefore, we believe that this distribution exists in our ethnic group and is not differed from other control groups in this area.

References

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3 Passarge E: Hardy-Weinberg equilibrium; in Passarge E (ed): Color Atlas of Genetics. New York, Thieme Verlag, 2001, p 158.

Fuu-Jen Tsai, MD
Departments of Medical Genetics and Pediatrics
China University Hospital, No. 2, Yu-Der Road
Taichung 404 (Taiwan)
Tel. +886 4 205 21 21, Fax +886 4 203 32 95
E-Mail d0704@hpd.cmch.org.tw