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Comments on: rs3761548 (C/A) and rs5902434 (del/ATT) polymorphisms of *Foxp3* gene in Iranian patients with migraine

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Dear Editor,

I read with interest the study by Dr Faraji et al. on "rs3761548 (C/A) and rs5902434 (del/ATT) polymorphisms of the Foxp3 gene in Iranian patients with migraine" [1]. The authors reported that the rs5902434 and rs3761548 genetic polymorphisms were associated with migraine susceptibility [1].

As mentioned by the authors, *FOXP3* (MIM: 300,292) is an X-linked gene located at band p11.23 [2]. In another correspondence regarding a similar article published in another scientific journal, I pointed out that unfortunately some researchers consider genetic polymorphisms of X-linked loci to be the same as polymorphisms of autosomal loci [3].

We know that women have two X chromosomes and men have one. This difference should be taken into account when estimating the allele frequency for polymorphisms located on the X chromosome. Obviously, women can have two similar (homozygous genotypes) or different (heterozygous) alleles of the polymorphism, whereas men have only one allele (hemizygous). In a sample where the number of women and men is equal to n_1 and n_2, respectively, the total number of alleles will be $2n_1+n_2$.

In the article by Faraji et al., some of the participants in both the patient and control groups were male and some were female. The authors of the article worked with 55 migraine patients (42 women, 13 men) and 80 healthy individuals (61 women, 19 men). According to Table 3 of the article under discussion, the total number of alleles for the rs5902434 and rs3761548 polymorphisms in the patient and healthy control groups was reported to be 110 and 160, respectively. In other words, these numbers correspond to twice the number of participants in the study groups. According to the number of women and men in each of the patient and control groups, the total number of alleles should be 97 ($=2\times42+13$) and 141 ($=2\times61+19$), respectively. This shows that Dr Faraji and colleagues counted two alleles for both men and women in their research, which is not correct. This fatal error made all their results inaccurate and unreliable. Finally, it should be mentioned that this error has unfortunately been made in many other articles which cannot be named for ethical reasons.

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Declarations

Ethics approval and consent to participate
Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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