It is feasible that the sex ratio of siblings may be associated with the development of autoimmune disease, as hormone concentrations are believed to affect the sex of offspring. Therefore, parents with low testosterone concentrations may be more likely to have female children, with these children being at an increased risk of developing RA because of their inherited tendency for low testosterone concentrations. If this hypothesis were true, it would also be expected that women with RA would themselves be more likely to have daughters instead of sons. Indeed, Deighton et al have previously reported such a finding, though numbers were small (16 daughters and seven sons). We have therefore investigated this relationship among a larger group of 94 women with RA. These women had provided pregnancy information and undergone HLA-DR typing for the purpose of another study (submitted for publication). The hypothesis was that if women with RA experience reduced concentrations of androgens, they might be expected to have an excess of daughters. Given that androgen concentrations may be partially regulated by HLA-DR status, the analysis was conducted separately for HLA-DR positive and negative offspring.

Overall, the 94 women had 202 children: 99 girls and 103 boys. The observed proportion of children that were daughters (0.49) was the same as that expected. When considered separately by HLA-DR status, however, there was an excess of sons among the HLA-DR4 negative mothers, and an excess of daughters among the HLA-DR4 positive mothers (table). The observation is associated with being HLA-DR4 positive and bearing a daughter was 2:1 (95% confidence interval 1:1 to 4:2). This therefore does appear to provide tentative evidence of a link between HLA-DR status and the gender of offspring, supporting a role for androgens in the aetiology of RA. These observations need to be repeated in other populations.

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