Short Communication

Erythrocyte acid phosphatase phenotype and gestational length: no relationship in a sample of 3001 births*

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Summary

Erythrocyte acid phosphatase (ACP,) phenotype was examined in 3001 Caucasian infants born at the University of Michigan Women’s Hospital. Contrary to reports from other studies, there was no relationship between the ACP, phenotype and risk of preterm birth in either the total sample or when the sample was subdivided by sex of infant.

gestational age; preterm birth; marker; erythrocyte acid phosphatase

In Caucasians, the erythrocyte acid phosphatase ACP, polymorphism is determined by three common alleles (P, P, P) at an autosomal locus. There are thus six electrophoretic phenotypes with a spectrum of enzymatic activity and physical and kinetic properties [1—5]. ACP, is suggested to have a physiological function as a flavin mononucleotide phosphatase and as such could have a role in regulating the levels of erythrocyte reduced glutathione and maintenance of erythrocyte integrity [6]. Bottini and coworkers have previously reported an association of gestational length and ACP, phenotype in

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a group of newborns studied at the University of Rome [7,8]. A sample of 608 infants was classified by ACP\_1 phenotype and by whether they were “preterm” (gestational length less than 37 weeks) [7]. The proportion of preterm births was higher in infants without the P\textsuperscript{b} allele than in infants with the P\textsuperscript{b} allele. When infants were stratified by sex, the relationship was apparent only in males. Bottini hypothesized that the ACP\_1 phenotype plays a role in determining gestational length in males and that the rate of preterm birth is lowest with a single dose of the P\textsuperscript{b} allele. In the present study, we explore these hypotheses in a sample of 3001 infants.

The sample of 3001 Caucasian live births consisted of infants born at the University of Michigan Women’s Hospital maternity service whose parents agreed to donate blood samples for another study [9]. Laboratory methods and allele frequencies for ACP\_1 and for 50 additional loci have been described elsewhere [10]. Hospital records of the infants were used to obtain gestational length, maternal age, race, presence of diabetes and smoking habit during pregnancy. Preterm status was taken as less than 37 weeks gestational length to agree with Bottini’s definition. The \( \chi^2 \) test was used, with statistical significance taken to be a \( P \)-value of 0.05 or less.

Table I shows the percentage of preterm births by ACP\_1 phenotype in the University of Michigan and Rome samples. In the Michigan sample, 10.8\% of infants without the P\textsuperscript{b} allele were preterm, compared to 11.4\% of infants with the P\textsuperscript{b} allele. When the sample was stratified by sex, the percentage of preterm births remained independent of the presence of the P\textsuperscript{b} allele (Table II). In the Rome sample, however, 11.5\% of infants without the P\textsuperscript{a} allele were preterm, compared to only 5.7\% of infants with the P\textsuperscript{b} allele (\( \chi^2 = 3.914, \text{d.f.} = 1, P < 0.05 \)). The discrepancy was apparent only in male infants (Table II).

We asked if the difference in the results of the Michigan study from those of Bottini in Rome could be due to environmental influences. For example, perhaps mothers in this sample who carried the P\textsuperscript{b} allele were more likely to be very young and hence more likely to deliver a preterm infant. There was no relation between allelic type and the maternal characteristics for which data were available (maternal age, smoking, or presence of diabetes), so these variables could not have influenced the result.
TABLE II

Rate of preterm birth by dose of P<sup>a</sup> allele and sex of infant.

<table>
<thead>
<tr>
<th>Dose of P&lt;sup&gt;a&lt;/sup&gt;,**</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td><strong>Males</strong></td>
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<tr>
<td>University of Michigan</td>
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</tr>
<tr>
<td>% preterm births (Total No. in group)</td>
<td>11.3</td>
<td>12.1</td>
<td>12.2</td>
<td>12.1</td>
</tr>
<tr>
<td>Rome</td>
<td></td>
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</tr>
<tr>
<td>% preterm births (Total No. in group)</td>
<td>15.0</td>
<td>3.6</td>
<td>6.5</td>
<td>6.3</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>University of Michigan</td>
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</tr>
<tr>
<td>% preterm births (Total No. in group)</td>
<td>10.4</td>
<td>9.9</td>
<td>11.6</td>
<td>10.6</td>
</tr>
<tr>
<td>Rome</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>% preterm births (Total No. in group)</td>
<td>7.9</td>
<td>5.5</td>
<td>7.0</td>
<td>6.4</td>
</tr>
</tbody>
</table>

*0 = AA, AC, CC; 1 = AB, BC; 2 = BB.
**Sex missing for 49 infants in University of Michigan sample.

The discrepancy in the results of the two studies may be due to significant differences in the two populations sampled. In the Rome sample, the rate of preterm birth is 6.4% compared to 11.3% in the University of Michigan sample (χ² = 12.849, d.f. = 1, P < 0.001). The University of Michigan hospital is a tertiary care center, so the higher preterm birth rate probably reflects the short gestation associated with problem pregnancies that are referred there. The differential in sample rates of preterm birth is consistent in both sexes (Table II).

There was also a significant difference in the distribution of the ACP<sub>1</sub> phenotype in female infants in the two samples (Table II). In the University of Michigan sample, 39.5% of the females were homozygous for allele P<sup>b</sup>, while 45.1% were heterozygous for the P<sup>b</sup> allele. The relationship was reversed in the Roman sample (47.7% and 38.8%, respectively; χ² = 6.422, d.f. = 2, P < 0.05 for comparison by dose of P<sup>a</sup> allele in the two samples). However, the difference in phenotype distribution could not be responsible for the observed differential in preterm birth rates in the two samples, since the rate in both was consistent across phenotypes for females in both samples. There was no statistically significant difference in the male phenotype frequencies of the two samples.

Gene frequencies in the two samples can be determined from data in Table I. The frequency of the P<sup>a</sup> allele is 0.33 in Michigan but only 0.27 in Rome, while the frequency of the P<sup>b</sup> allele is higher in Rome (0.67 vs. 0.63). The difference in gene frequencies in the two samples is statistically significant (χ² = 22.055, d.f. = 2, P < 0.001) The University of Michigan sample appears to be in Hardy-Weinberg equilibrium, while the Rome sample does not (χ² = 11.298, d.f. = 5, P < 0.05 for comparison of observed and expected phenotypes).
The differing rates of preterm birth, gene frequency and phenotype distribution in the two studies suggest that the populations are not comparable, and that there are other factors that influence gestational length independent of, or in concert with, ACP, phenotype. For example, the Michigan population is almost devoid of glucose-6-phosphate dehydrogenase (G6PD) deficiency. In a subset of this sample, only three of 908 male newborns had marginal G6PD deficiency (activity 15—25% of normal) [11]. The level of ACP, activity (and therefore genotype) has been reported to be inversely related to the erythrocyte concentration of the enzyme cofactor, flavin adenine dinucleotide (FAD) and, therefore, the basal activity of the key erythrocyte enzyme, glutathione reductase. Increased ingestion of the vitamin riboflavin, the precursor for FAD, would undoubtedly tend to diminish the role of ACP, in the regulation of glutathione reductase activity, reduced glutathione levels and erythrocyte integrity. The large size of our sample, however, leaves little doubt that ACP, phenotype is unrelated to gestational length in the University of Michigan population from which it is drawn.

References