

BIRTHWEIGHT OF INFANTS WITH PHENYLKETONURIA*M. Máté, C. Somogyi, and L. Szabó*

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Abstract: *The birthweights of 113 Hungarian children with PKU (56 boys and 57 girls) were compared with the birthweights of controls from the Hungarian Standard. The mean value for boys was 3188.9 g (SD = 345.0), which is 30.3 g lower than the control's. The mean value for girls was 3241.0 g (SD = 366.8), which is 149.8 g higher than the average value of the controls. 16.8% of the newborns with PKU (11 boys and 8 girls) had a birthweight under the 10th percentile (10.98% in controls). The lower rate of pre-term deliveries (5.7% in PKU, 14.4% in controls) and still-births (0.4% in PKU, 0.8% in controls), furthermore spontaneous abortion (11.8% in PKU, 13.3% in controls) shows, that a heterozygote advantage can be presumed in PKU, which maintains the high frequency of homozygotes for PKU, but the PKU gene does not influence unambiguously the birthweight.*

Key words: *Infants with phenylketonuria; Birthweight.*

Introduction

Since 1968, when direct screening of the newborns was introduced the incidence of PKU in Hungary found to be 1/8302 live births (Szabó–Somogyi–Máté 1985). Furthermore a number of genetic hyperphenylalaninemias have become known. Before the introduction of dietary treatment the reproductive fitness of homozygotes for the PKU gene was very close to zero, because in untreated classical PKU the I.Q. is almost always very low (Woolf 1986, Vogel 1984). The observed frequency of homozygotes for PKU is much too high to be maintained by fresh mutations, which typically have a maximum frequency of 1 in 100 000. The most plausible reason for this phenomenon is heterozygote advantage, well-known for instance for the sickle-cell gene, leading to a higher reproductive fitness. The nature of this possible advantage for PKU heterozygotes is still unknown. Although heterozygotes for PKU do not deviate visibly from normal homozygotes, recognizable peculiarities have been reported: they show deviations in I.Q., for instance (Thalhammer et al. 1977), and have higher fasting plasma phenylalanine levels (Kang–Paine 1963, Woolf 1986). The best way to find such a heterozygote advantage appears to be the direct comparison of effective fertility between heterozygotes and normal homozygotes. It is believed that the higher plasma phenylalanine level in heterozygotes, which increases during pregnancy (Kang–Paine 1963), protects the foetus against protein deficiency or toxic substances (Anonymous 1977, Woolf et al. 1975).

The advantage might be expressed in a lower rate of abortions and still-births, fewer problems during pregnancy and at birth, and higher average birthweights, too (Woolf et al. 1975). On the other hand there are reports of an increased rate of reproductive incompetence manifest by abortions, bleeding during pregnancy, pre-term births, lower average birthweights and more still-births in heterozygotes for PKU (Blyumina 1974, Saugstad 1972).

The present work gives further informations about the birthweights of Hungarian children suffering from PKU and the distribution of their percentile values compared with controls from the Hungarian Standard (Joubert 1983).

Further data are presented about the rates of abortions and still-births, the total number of pregnancies per mother, about the rate of bleeding and other problems during pregnancy (pregnancy of risk), premature deliveries and perinatal or postnatal problems.

Materials

The material analysed includes 113 (56 boys and 57 girls) offsprings with PKU from 104 obligatory phenylketonuric heterozygous mothers. The children are from the material of the Screening Centre in Budapest. They were born between 1972 and 1986 in Western-Hungary or in Budapest.

Results

Birthweights were analysed for 51 boys and 50 girls with PKU. Eight newborns (2 boys, 6 girls) of pre-term, and four (3 boys, 1 girl) of post-term deliveries were excluded. The average birthweights are presented in Table 1.

The mean value for boys with PKU was 30.3 g lower than the normal group's birthweight, that of girls 149.8 g higher, and this difference was significant.

19 newborns (16.8%) were found with a birthweight under the 10th percentile and seven (6.2%) over the 90th percentile. The distribution of the levels above the 50th percentile was 42.9% in the boys and 54.4% in the girls (Table 2).

Table 3 gives the comparison of the fertility between 104 obligatory heterozygous mothers and normal homozygotes. The total number of pregnancies is higher in the heterozygous mothers. Furthermore the rate of abortions, pre-term deliveries, still-births, pregnancies of risk and complicated deliveries is lower than in the general population.

Table 1. Comparison of average birthweights (g)

	Boys		Girls	
	Hungarian Standard	PKU	Hungarian Standard	PKU
n	448574	51	421319	50
x (g)	3219.2	3188.9	3091.2	3241.0*
SD	325.3	345.0	312.3	366.8

* $p < 0.05$

Table 2. Percentile values of birthweights from children suffering from PKU

Percentile	Boys (%)	Girls (%)
< 10	14.4	10.2
> 50	42.9	54.4
> 90	7.0	5.4

Table 3. Comparison of the fertility between heterozygote mothers and normal homozygotes

	Hungarian average population	Obligatory heterozygous mothers (n=104)
total number of pregnancies per mother	2.2	2.3
spontaneous abortions	13.3%	11.8%
still-births	0.8%	0.4%
pre-term deliveries	14.5%	5.7%
pregnancy of risk	29.0%	7.9%
complicated deliveries	7.5%	4.7%

Discussion

Our results are in good agreement with observations of other authors. Cabalska et al. (1982) in Poland, Rothman-Pueschel (1976) in USA and Smith et al. (1978) found only small differences in birthweight, too. Only Saugstad (1972) observed in a Norwegian sample an increased birthweight, which may be an effect of one or two large sibships, in which birthweights were high. Our own data suggest, that the PKU gene does not influence unambiguously the birthweight of infants with PKU.

On the other hand it seemed possible that the slightly higher phenylalanine concentration in the blood of pregnant heterozygotes might favour foetal and neonatal survival, particularly in protein malnutrition (Woolf et al. 1975). This fact leads to a lower proportion of spontaneous abortions and still-births in heterozygotes for PKU, which has been found by other authors, too (Cabalska et al. 1982, Smith 1978, Woolf 1986, Woolf et al. 1975).

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