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BIRTH WEIGHT OF IRANIAN CHILDREN WITH PHENYLKETONURIA

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To assess whether birth weight is affected in Iranian patients with phenylketonuria, birth weights of 118 patients with phenylketonuria were compared with 264 healthy controls matched by gestational age and sex, and with patients unaffected siblings. The mean (±SD) birth weight of phenylketonuria patients and control group was 3199.5 (±554.5) and 3260.3 (±483.2) grams, respectively. The mean birth weight of phenylketonuria patients was by 60.7 lower as compared with controls (p=0.27). There was no significant correlation between disease severity and phenylketonuria patient birth weight (p=0.55). The mean (±SD) birth weight of 59 phenylketonuria patients and their siblings was 3193.2 (±568.6) and 3083.9 (±514.0)g, respectively. The mean birth weight of phenylketonuria patients was by 109 g greater as compared with their siblings (p=0.271). Birth weight of Iranian phenylketonuria patients was not significantly lower as compared with their healthy siblings and normal population. Although control infants had a slightly greater birth weight than phenylketonuria infants and phenylketonuria infants had a slightly greater birth weight than their unaffected siblings, the difference was not statistically significant. Furthermore, birth weight was not affected by the disease severity.

Descriptors: PHENYLKETONURIAS; BIRTH WEIGHT; IRAN

INTRODUCTION

Phenylketonuria (PKU) is an autosomal recessive metabolic disorder in which the essential amino acid phenylalanine cannot be converted into tyrosine, leading to the accumulation of toxic metabolites. The excess amount of phenylalanine causes skin disorders, neurologic disorders, somatic development disorders, etc. (1).

Toxic metabolites are usually removed by the placenta and metabolized by the mother, thus they do not harm the fetus and fetus usually has normal intrauterine development (2).

While lower birth weight has been reported in some studies (3, 4), many others did not find any significant reduction in birth weight of children with PKU in comparison to the normal population or their unaffected siblings (5-10).

This study was performed to assess whether Iranian PKU patients have a lower birth weight than their siblings or the normal population.

MATERIALS AND METHODS

Parents of 118 Iranian PKU patients (born 1985 to 2010) agreed to participate in the study. Patients were gathered from the metabolic clinic of the Mofid Children Hospital, Tehran, Iran.

We considered a case as a phenylketonuric patient if his/her pretreatment blood phenylalanine concentration was greater than 6 mg/dL by fluorometeric method (1).

All of the cases had a gestational age (GA) of 37 to 41 weeks, except for one with GA of 36 weeks. Data on birth weight were asked just from mothers, and they were asked to write down the birth weight if they recalled the exact birth weight. We compared our patients' birth weight with a control group of 264 subjects, matched by gestational age and sex. The controls were collected from the same hospital and did not have a history of any chronic or underlying disease.

Furthermore, we compared our patients' birth weight with their siblings. Statistical analysis was performed by independent sample t-test and p values <0.05 were considered significant.

We also studied the correlation between the severity of the disease and birth weight of patients by analyzing the correlation of blood pretreatment phenylalanine concentrations and birth weight of patients by Pearson correlation test.

A written informed consent was obtained from parents of the patients and the study protocol was reviewed and approved by the Mofid Children Hospital Ethics Committee.

RESULTS

The mean birth weight of 118 patients (62 female and 56 male) was 3199.5 g

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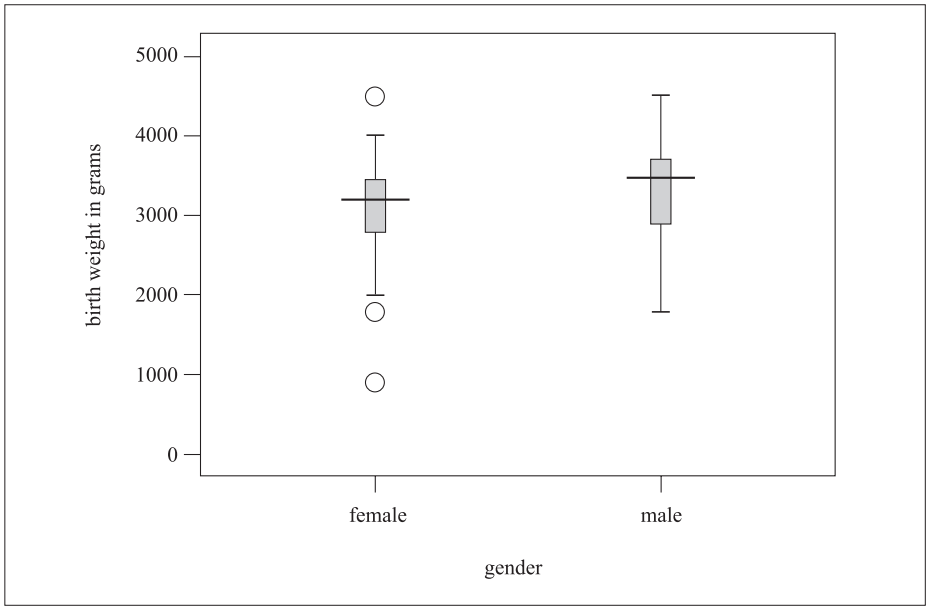

Figure 1. Birth weight of phenylketonuria patients according to gender

(range: 900 to 4500 g), with median of 3250 g. About 6.8% of patients had low birth weight (birth weight less than 2500 g). The mean (±SD) birth weight of females and males was 3098.5 (±580.4) and 3311.4 (±506.1) g, respectively (p=0.03) (Figure 1). Also, a remarkable point was that 11.3% of girls *versus* 1.8% of boys had low birth weight (Pearson χ^2 value = 0.04).

The mean birth weight of our control group (147 females and 117 males) was 3260.3 g. The birth weight of PKU patients was by 60.7 g less than of the controls. The independent sample t-test yielded no significant association between the mean birth weight of cases and controls (p=0.27) (Table 1).

In two patients, data on pretreatment phenylalanine concentration were not available, however, there was no significant correlation between pretreatment blood phenylalanine concentrations and birth weight (r=-0.56; p=0.55).

Of 118 patients, 80 patients had healthy siblings (at least one and maximum three). We just had access to birth weight of siblings of 59 patients. We calculated the mean sibling birth weight of each family and we compared the patient mean birth weight and the sibling mean birth weight by paired sample *t* test. The birth weight of PKU patients was by 109 g greater than of their siblings (p=0.271). The result was not statistically significant (Table 2).

Table 1. Mean and standard deviation (SD) of birth weight in phenylketonuria (PKU) patients and control group (g)

	n	Mean value	SD	P value
PKU	118	3199.5	554.5	0.27
Control	264	3260.3	483.2	

Table 2. Mean and standard deviation (SD) of birth weight in phenylketonuria (PKU) patients and their siblings (g)

	n	Mean	SD	P value
PKU	59	3193.22	568.62	0.271
Siblings	59	3083.90	514.06	

DISCUSSION

Our study showed that there was no significant difference between the birth weight of PKU patients, their siblings and normal population. Although control infants had a slightly greater birth weight than the PKU infants and PKU infants had a slightly greater birth weight than their unaffected siblings, the difference was not statistically significant, so this finding might have been quite accidental.

Rothman and Pueschel revealed that there was no significant reduction in birth weight of children with PKU in 40 sibships. They did not find the normal population to have lower birth weight than the siblings either (9). In England, Smith et al. found that there was no significant difference between birth weight of 56 children with PKU, their siblings and the British general population.

Another study in the UK examined birth weight of 1886 children with PKU. In comparison with normal children born in the 1970s and 1980s, no difference was found between PKU children and normal population. Furthermore, there was no correlation between the severity of the disease and birth weight of PKU children (10). Bianca et al. studied 260 Sicilian children with hyperphenylalaninemia, who showed no significant difference from the control group of 963 newborns matched by gestational age either (8).

In Norway, Saugstad compared 53 PKU children with their 86 siblings and showed the patient birth weight to be by about 500 g lower than in their siblings. On the other hand, the author showed that the sibling birth weight was by 300 g greater than in the Swedish normal population (4). In 1977, the same author confirmed her hypothesis of low birth weight in these children on 49 patients and 86 siblings; however, the sibling mean birth weight was higher than in 135 695 Norwegian neonates (11). Saugstad stated that the low birth weight in PKU children was related to the increased perinatal morbidity and low coherent achievement (12).

After adjustment for confounding variables, Verkerk et al. found that birth weight of children with PKU was by 141 g lower than the standards of the Dutch general population (Kloosterman study) and by 103 g lower than the SMOCC reference (3). Smith et al. believe that the finding of Saugstad, which states that the sibling birth weight is above the standards for the general population might be by chance (5). Crockett et al. conclude that low birth weight in children with PKU and their siblings is due to their maternal genotype and not the disease effect (6, 7).

In our study, we found no significant birth weight difference between PKU patients and control group, which confirmed the results of previous studies. However, the number of cases compared with their siblings (59) was lower than the total number of patients (n=118); the patient birth weight was not significantly different from their siblings. Like Tillotson et al., we did not find any correlation between birth weight of our patients and disease severity (10).

LIMITATIONS

We could not reach birth weight of all siblings and this might increase the chan-

ce error in our study. However, we asked mothers to write data on birth weight they were sure, thus a recall bias might have happened in the study. The lack of data on prenatal care and pathologic conditions is one of our study limitations; however, as PKU infants had a slightly greater birth weight than their unaffected siblings, we may presume there were no pathologic conditions.

Authors declare no conflict of interest.
Autori izjavljuju da nisu bili u sukobu interesa.

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S a ž e t a k

POROĐAJNA MASA IRANSKE DJECE S FENILKETONURIJOM

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Cilj studije je bio procijeniti postoji li razlika u porođajnoj masi u djece s fenilketonurijom u Iranu u odnosu na kontrolnu skupinu. Porođajna masa 118 bolesnika s fenilketonurijom uspoređena je s porođajnom masom 264 zdrave kontrolne osobe jednake gestacijske dobi i spola, kao i s masom nezahvaćene braće/sestara bolesnika. Srednja (±SD) porođajna masa bolesnika s fenilketonurijom i kontrolne skupine bila je 3199,5 (±554,5), odnosno 3260,3 (±483,2) grama. Porođajna masa bolesnika s fenilketonurijom bila je za 60,7 grama manja u odnosu na kontrole (p=0,27). Nije bilo značajne korelacije između težine bolesti i porođajne mase bolesnika (p=0,55). Srednja (±SD) porođajna masa 59 bolesnika s fenilketonurijom i njihove braće/sestara bila je 3193,2 (±568,6) odnosno 3083,9 (±514,0) grama. Porođajna masa bolesnika s fenilketonurijom bila je za 109 grama veća od one njihove braće/sestara (p=0,271). Porođajna masa iranskih bolesnika s fenilketonurijom nije značajno niža od one njihove zdrave braće/sestara i zdrave populacije. Iako je porođajna masa kontrolne dojenčadi bila nešto veća od one bolesnika s fenilketonurijom, a dojenčad s fenilketonurijom je imala nešto veću porođajnu masu od njihove braće/sestara, razlika nije bila statistički značajna. Uz to, težina bolesti nije imala utjecaja na porođajnu masu.

Deskriptori: FENILKETONURIJE; POROĐAJNA MASA; IRAN

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