Physical growth of preterm girls with visual impairment

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ABSTRACT The aim of this study was to estimate pubertal age and to assess the level of physical development of preterm girls with defective vision. The study material – anthropometric data (body height and weight, BMI) and information on the age of menarche were collected from 155 subjects with defective vision (partially sighted and blind). Median age at menarche was estimated by probit analysis. The girls, ranging in age from 7-18 years, attended Centers for Blind and Partially Sighted Children in Wroclaw and Cracow (Poland). 22% of the subjects were prematurely born, were born with low birth mass and their sight defect diagnosed as retinopathy due to prematurity (ROP). The girls with ophthalmic impairments were shorter and lighter than their age peers from the reference data. Blind girls reached pubertal age 2 months earlier than the partially sighted (Me=13.31 and Me=13.44) and, the preterm subjects entered puberty 6 months earlier than the full-term girls, irrespective of degree of defect (Me=12.93 and Me=13.42, respectively). The results suggest that earlier puberty is associated with visual impairment. The results show also that irrespective of the degree of defect, preterm girls reach menarche significantly earlier than those who were full-term. It seems possible that mechanisms responsible for earlier puberty in the preterm subjects and with low body mass play an important role in sexual maturation in girls with sight dysfunction. There appears to be a need to pursue further studies in this sphere.

KEY WORDS: preterm born girls, age at menarche, sight dysfunction, retinopathy of prematurity

Very few studies confirm earlier puberty in girls with sense organ impairment than in healthy girls [ZACHARIAS and WURTMAN 1964; MALINA and CHUMLEA 1977; BUDAY 1981; ŁUCZAK 1992; BUDAY and KAPOSI 1995; UMLAWSKA 2000, 2006]. The age of menarche tended to be interpreted usually in terms of the influence of the degree of sight or hearing defects and its etiology. These findings reveal with regularity that the more serious the degree of dysfunction, the earlier the menstruation age, and in case of sight
deficiency, emphasizes the important role of the pineal gland in this process. The earlier age of menarche in girls corresponding to defective vision may be the outcome of therapies applied during the treatments such as radiation of the central nervous system or brachysurgeries [UMLAWSKA 2000]. Two of the studies report cases of earlier menarche in a sample of preterm girls who suffered from postnatal sight defects; however, this phenomenon has not as yet been interpreted [ZACHARIAS and WURTMAN 1964, UMLAWSKA 2000].

The relationship of low birth mass to gestational age and postnatal growth has been known as Barker’s hypothesis. The research states that low birth mass in respect of gestational age predisposes the subjects to visceral obesity, coronary heart disease, dyslipidemia, hypertension, and type 2 diabetes mellitus at adult age [BARKER 1999, LUCAS and al. 1999, BARKER 2002, OZANNE and HALES 2002, HOFMAN et al. 2004]. It has recently been shown that low birth mass correlates with sexual maturity and reproduction, e.g., earlier pubertal onset [PERSSON et al. 1999, IBANEZ et al. 2000b, ADAIR 2001, KOZIEL and JANKOWSKA 2002]. These reports encourage studies on the relationships mentioned above in the group of girls with sight deficiency.

The purpose of this study was to estimate pubertal age and to assess the level of physical development of preterm girls with sight deficiency.

**Materials and methods**

Body height and weight were collected from 155 girls aged 7-18 years, with various sight defects. The subjects were recruited from Centers for Blind and Partially Sighted Children in Wroclaw and Cracow, Poland. Body height and weight were measured according to the method described by MARTIN and SALLER [1957-1959] and the Body Mass Index BMI (kg/m²) was used as an index of relative weight. Median age at menarche was estimated by probit analysis. The number of examined girls and menstruating girls in subsequent age-groups is presented in Table 1.

<p>| Table 1. Number of examined girls and menstruating girls in subsequent age. |</p>
<table>
<thead>
<tr>
<th>Age group</th>
<th>No. of subjects</th>
<th>No. of menstruating girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>13</td>
<td>18</td>
<td>12</td>
</tr>
<tr>
<td>14</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>15</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>16</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>17</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>18</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>155</strong></td>
<td><strong>89</strong></td>
</tr>
</tbody>
</table>

Medical records in both Centers provided the information on the degree of sight defect, reasons and surgeries as well as other therapies employed in their treatment. The majority of the subjects (63%) were girls with a high degree of sight defect, while the remaining 37% were blind with or without light perception. From the etiology of sight impairment, subjects were divided into three categories. The most frequently cited reason for sight dysfunctions were prenatal acquired congenital defects and indeed they constituted the first category as 48% of the subjects’ sight defects were observed upon birth or in early childhood
and ophthalmologic anamnesis had excluded the occurrence of defective vision in the closest family. Included among the prenatal congenital defects were optic atrophy, cataract, and retinal degeneration. The second category comprised 30% of subjects with defects acquired postnatally due to the eyeball traumas, retinopathy of prematurity (ROP) or cancer. The third category consisted of 22% subjects with hereditary defects, such as retinal degeneration, cataract or optic atrophy.

Although the medical records did not provide detailed information on the subjects (e.g., body length and mass at birth), they provided information on perinatal complications and preterm deliveries, revealing that 22% of the subjects were prematurely born (between week 26 and 35 of pregnancy), therefore probably with low body mass, nurtured in incubators after birth and having sight defects following ROP. It is believed that nowadays 5.8% of preterm infants born in Poland are affected with ROP [PROST 1998]. ROP is the impairment of premature blood vessels in the retina resulting from a disturbed balance between the oxidative and anti-oxidative processes in this tissue [SMITH 2003]. A strong relationship between the degree of an infant prematurity and the incidence of this defect has been observed and, thus, the defect is more serious in subjects having low birth mass [O’CONNOR et al. 2003]. In preterm subjects with very low birth weight (VLBW, below 1500 g), and in particular with extremely low birth weight (ELBW, below 1000g), the anti-oxidation systems are underdeveloped and the retina amasses free radicals which preclude the correct development of its vascularization, resulting, in consequence, in its ablation.

In extreme preterm infants, the vascular endothelium in the retina can be damaged even by a partial arterial pressure since an optimal pressure is indispensable for proper oxygenation of the central nervous system. It was revealed that in the subjects with body mass below 1000g blindness occurs in 11.5% of them whereas in children over 2000g blindness is almost non-existent. ROP prevention includes screening of partial oxygen pressure in the infant’s blood in the incubator. The treatment most frequently involves laser coagulation of the peripheral non-vascular retinal areas or cryotherapy [PROST 1998].

Without knowledge of the birth mass of the subjects, yet knowing the reason underlying the retinopathy in the preterm cases, we assumed that the girls who suffered from this illness were born with VLBW or with ELBW.

Anthropometric data were expressed as SDS for chronological age and sex according to Polish references (PALCZEWSKA and NIEDZWIEDZKA 2001). The differences in standardized means of somatic traits between the girls with visual impairment and the sample of healthy children were tested by the Student’s t-test for two samples with equal variance. The association between premature or full-term cases and the degree of sight defect was tested using $\chi^2$ test for qualitative variables. The distributions of analyzed traits were assessed by Shapro-Wilk test. The Wilcoxon test (after Gehan) was employed to assess the statistical significance of the differences between mean values of menarche age. This test is used to compare mean values calculated by means of a probit method. Statistical significance was accepted at $p < 0.05$. Analyses were carried out using STATISTICA 6.0.
Results

The girls with sight defects were shorter and lighter than the reference group. They were more deprived in height than in weight and, therefore, tended to be more thickset (Table 2).

Among 125 girls aged 11-18 years, 89 (71%) were menstruating; the mean age of menarche was 13.35±1.95 years. Blind girls menstruated almost 2 months earlier than those with defective vision, but the difference was statistically negligible (Table 3). Among the group of 89 menstruating girls, 16 subjects (18%) were preterm, and their sight defect had ensued from ROP. In the preterm girls, the onset of puberty was 6 months prior to the puberty of the term-born, making the difference statistically significant (Table 4).

No significant differences in somatic traits were found between preterm and term-born menstruating girls but there was a tendency to a more thickset body build in the preterm subjects (Table 2).

The relationship between the prematurity or full-term date and the degree of sight defect was analyzed and shown to be statistically significant ($\chi^2 = 13.85$, df = 1, $p < 0.001$). Among the preterm subjects, girls with their blindness resulting from severe cases of ROP prevailed. It was observed that among 16 menstruating preterm girls 6 were poorly-sighted subjects and 10 were blind, and irrespective of the degree of sight defect, all of them had attained puberty before the rest, i.e., at around 13 years of age. Preterm girls with sight defects menstruated much earlier than full-term girls with sight dysfunction irrespective of their disability.

<table>
<thead>
<tr>
<th>Somatic traits</th>
<th>$\bar{x}$</th>
<th>SD</th>
<th>min-max</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body height</td>
<td>-0.88</td>
<td>1.28</td>
<td>-6.23–2.31</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Body mass</td>
<td>-0.27</td>
<td>1.29</td>
<td>-2.97–5.81</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>BMI</td>
<td>0.16</td>
<td>1.39</td>
<td>-2.59–8.11</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Table 3. Age at menarche in the examined girls (Wilcoxon test).

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Me</th>
<th>N</th>
<th>SD</th>
<th>W-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partially sighted</td>
<td>13.44</td>
<td>67</td>
<td>2.48</td>
<td></td>
</tr>
<tr>
<td>Blind</td>
<td>13.31</td>
<td>22</td>
<td>2.48</td>
<td>0.15</td>
</tr>
<tr>
<td>Total</td>
<td>13.35</td>
<td>89</td>
<td>1.95</td>
<td></td>
</tr>
</tbody>
</table>

p > 0.05

Table 4. Age at menarche in preterm and term girls (Wilcoxon test).

<table>
<thead>
<tr>
<th>Girls born</th>
<th>Me</th>
<th>N</th>
<th>SD</th>
<th>W-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm</td>
<td>12.93</td>
<td>16</td>
<td>2.87</td>
<td></td>
</tr>
<tr>
<td>Term</td>
<td>13.42</td>
<td>73</td>
<td>2.30</td>
<td>1.90*</td>
</tr>
</tbody>
</table>

* p < 0.05
Discussion

Adverse conditions for fetal growth, caused by the mother’s undernutrition, placental dysfunction or other factors, are concomitant with the infant’s low birth mass. Preterm birth and low mass have numerous health consequences both in childhood and at adult age, known as the Metabolic Syndrome [BARKER 1999]. HALES and BARKER [1992] postulated The Thrifty Phenotype Hypothesis, according to which infants with low birth mass adapt themselves to undernutrition in the prenatal period and maximize chances of their postnatal survival period [OZANNE and HALES 2002, HOFMAN et al. 2004]. Fetal undernutrition replaced by overnutrition after birth predisposes the organism to obesity, type 2 diabetes mellitus, coronary heart disease, and many other afflictions [BARKER 2002]. The above-mentioned adaptation of the organism to demanding conditions in utero involves altering metabolism and endocrine set points which continue through the postnatal period and cause alterations in insulin metabolism leading to obesity and type 2 diabetes mellitus [HOKKEN-KOÈLEGA 2002]. Such alterations regard also other hormonal axes [OZANNE and HALES 2002].

In early childhood, preterm subjects manifest a higher level of growth hormone (GH) probably due to a low level of insulin-like growth factors (IGF-1) which are involved in growth process by affecting the osseous tissue and their binding proteins (IGFBP-3). Low levels of IGF-1 and IGFBP-3 and short stature in prepubertal subjects born with low mass were observed by CUTFIELD et al. [2004]. The authors stated that the results testify to persistent partial GH resistance in those children. Other studies, however, revealed GH deficiency in children born with low body mass and the need for GH replacement therapy [RAPAPORT 2004].

The appropriate level of IGF-1 is considered indispensable for normal growth of the retinal vasculature. A low level of IGF-1 in preterm subjects causes incorrect vascularisation of the retina and ROP [O’CONNOR et al. 2003].

Female subjects manifested short stature when compared with their normally sighted peers (Tables 2, 5). The precise reason for this phenomenon is not easy to determine although it might to be associated with the therapies used to treat sight defects that disturb the proper functioning of the hypothalamus-pituitary axis (brachysurgery), illness- and disability-connected stress, or preterm birth. Studies of postnatal growth of children born with low body mass show that the occurrence of catch-up growth in more than 80% of children aged 2-3 years [HOKKEN-KOÈLEGA et al. 1995, HOKKEN-KOÈLEGA 2002]. JAQUET et al. [2004]
observed stature deficiency in adulthood among people born with low body mass as their mean body height was -0.7 SD, and in 10% of subjects this value fell below -2 SD in reference to the normal population mean.

It is thought that catch-up growth of body mass is caused by rapid growth of adipose tissue rather than an increment in stature reflected by BMI, especially in early childhood [LÉVY-MARCHAL et al. 2004]. In our data the fact that there were no significant differences in standardized values of weight and BMI showed that there was no difference between the menstruating girls born preterm and term. However there was a tendency to a more thickset body build in the preterm subjects (Table 5).

The subjects born prematurely with defective sight showed no significant differences in height and weight when compared with the full-term subjects, yet matured 6 months earlier irrespective of the degree of dysfunction (Table 4). The relationship between low birth mass and pubertal age has not yet been well documented. Some authors [PERSSON et al. 1999, IBANEZ et al. 2000b], however, indicated an earlier age of onset of puberty for these girls. IBANEZ et al. [2000a] revealed that girls born with low body mass reached maturation 1.5 years earlier than full-term girls (11.3±0.3; 12.9±0.2 years, respectively), but were also shorter by over 5 cm (153.0±1.8; 158.3±1.0 cm). A 4-month earlier menarche age was observed in Swedish girls by PERSSON et al. [1999]. Girls with low birth-weight showed not only an earlier menarche, but also hyperinsulinism, precocious pubarche, exaggerated adrenarche and polycystic ovary syndrome (PCOS) [IBANEZ et al. 1999, IBANEZ et al. 2000b]. Girls with reduced prenatal growth are thought to experience accelerated puberty, earlier menarche and shorter adult height. There are no observed neuro-hormonal mechanisms compensating for the early pubertal onset – girls with normal birth weight tend to progress slowly through puberty with a normal onset of menarche and a normal final height [IBANEZ et al. 1999].

Low body mass affects also reproduction. In girls with low birth mass, USG evidenced smaller ovaries could be a reason for more frequent anovulatory cycles [IBANEZ et al. 2000b]. It is also possible that intrauterine growth retardation may disturb ovarian functioning because of hypersecretion of follicle-stimulating hormone (FSH) [IBANEZ et al. 2000b, IBANEZ et al. 2002].

**Conclusion**

The obtained results suggest that visual impairment is associated with earlier onset of puberty. The results show also that, irrespective of the degree of defect, preterm girls reach menarche significantly earlier than those who were full-term. It seems possible that mechanisms responsible for earlier puberty in the preterm subjects and which have low body mass play an important role in the sexual maturation of girls with sight dysfunction. There appears to be a need to pursue further studies in this sphere.

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Streszczenie

Celem opracowania była ocena poziomu rozwoju fizycznego dziewcząt z dysfunkcją narządu wzroku urodzonych przedwczesnie. Badania dotyczyły 155 osób dziewcząt w wieku 7-18 lat będących uczennicami Ośrodków Szkolno-Wychowawczych Dzieci Niewidomych we Wrocławiu i w Krakowie. Pośród badanych 37% stanowiły osoby niewidome, a 63% osoby niedowidzące. Wykonano pomiary wysokości i masy ciała oraz obliczono wskaźnik masy ciała BMI. Wiek menarche ustalono metodą status quo, pytając badane dziewczęta o obecność lub brak miesiączki. Wśród badanych, 22% stanowiły dziewczęta urodzone przedwczesnie (między 26 a 35 tygodniem ciąży), przebywające po porodzie w inkubatorze, a ich wada wzroku była następstwem retinopatii wczesniaków.

Dane pomiarowe poddano zabiegowi standaryzacji względem grupy referencyjnej. W obliczeniach wykorzystano test t-Studenta, test Wilcoxona według Gehana oraz test $\chi^2$. Dziewczęta z wadami wzroku okazały się istotnie statystycznie niższe i lżejsze od swoich widzących rówieśniczek z grupy porównawczej. Odchylenia minus były większe w przypadku wysokości ciała aniżeli masy ciała, dziewczęta z dysfunkcją narządu wzroku cechowała więc bardziej krępą budowę ciała (tab. 2). Nie zaobserwowano istotnych statystycznie różnic w wartościach rozpatrywanych cech pomiędzy dziewczętami urodzonymi przedwczesnie i w prawidłowym terminie (tab. 5). Średni wiek menarche badanych wyniósł 13,35±1,95. Dziewczęta niewidome miesięczkowały prawie 2 miesiące przed niedowidzącymi (odpowiednio 13,31 i 13,44 lat), zaś urodzone przedwczesnie – 6 miesięcy przed urodzonymi w terminie (12,93 i 13,42 lat) (tab. 3, 4).

Redukcja okresu prenatalnego w przypadku badanych dziewcząt przyczyniła się do powstania wady wzroku, ale wydaje się, że nie pozostała bez wpływu na ich rozwój postnatalny, a zwłaszcza stosunkowo wczesny wiek pokwitania. Uzyskane wyniki wskazały bowiem, iż niezależnie od stopnia nasilenia wady wzroku, dziewczęta urodzone przedwczesnie miesięczkowały istotnie wcześniej od urodzonych w terminie. Niewykluczone więc, iż mechanizmy związane z wcześniejszym pokwitaniem urodzonych przedwczesnie i z niską urodziniową masą ciała odgrywają w przypadku dziewcząt z dysfunkcją wzroku również ważną rolę, jak rozpatrywany zazwyczaj w badaniach, stopień nasilenia wady wzroku.