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Maternal age as a risk factor for cerebral palsy

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ABSTRACT: The relationship between maternal age and the occurrence of cerebral palsy is still highly controversial. The aim of the study was to examine the effect of maternal age on the risk of CP development, taking into account all significant risk factors and the division into single, twin, full-term, and pre-term pregnancies.

The survey covered 278 children with CP attending selected educational institutions in Poland. The control group consisted of data collected from the medical records of 435 children born at Limanowa county hospital, Poland. The analyses included socio-economic factors, factors related to pregnancy and childbirth, and factors related to the presence of comorbidities and diseases in the child. Constructed logistic regression models were used for statistical analyses.

For all age categories included in the estimated models (assessing the effect of demographic factors on the development of CP), only the category of ≤24 years of age (in the group of all children) was significant. It was estimated that in this mother's age category, the risk of CP is lower (OR 0.6, 95% CI: 0.3–1.0) in comparison to mothers aged 25-29 ($p = 0.03$). However, estimation with the use of a complex logistic regression model did not show any significant effect of maternal age on the incidence of CP in groups from different pregnancies types.

It became apparent that maternal age is a weak predictor of CP, insignificant in the final logistic regression model. It seems correct to assume that the studies conducted so far, showing a significant effect of maternal age in this respect, may be associated with bias in the estimators used to assess the risk of CP due to the fact that other important risk factors for CP development were not included in the research.

KEY WORDS: Cerebral palsy, twin birth, pre-term birth, term birth

Introduction

According to the definition formulated in 2007, cerebral palsy (CP) is a group of permanent developmental disorders affecting the motor system and body posture, resulting in limitations of motor activity. They are associated with

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non-progressive disorders emerging in the developing fetal or neonatal brain. Motor disorders are often accompanied by disorders of sensation, perception, cognition, communication, and behavior, as well as epilepsy and secondary musculoskeletal problems (Rossenbaum et al. 2007; Kuban et al. 2008; Himmelmann et al. 2010). To a large extent, the occurrence of CP is determined by the maturity of the central nervous system at the time of the action of unfavorable factors, which makes it difficult to demonstrate a relationship between the etiology and the clinical picture of CP (Jóźwiak S. 2001; Jacobsson and Hagberg 2004).

The complexity of diagnosis and disease symptoms, as well as the complex etiology and pathogenesis of CP are the main reasons why the incidence rate of CP on a global scale is not precisely known. According to the literature data, the prevalence rate of CP ranges from 1 to even 5 cases per 1000 live births (Kiely et al. 1981; Johnson and Catterson 1988; Platt and Pharoah 1995; Colver et al. 2000; Jóźwiak M. 2001; Kwolek et al. 2001; Zgorzalewicz et al. 2001; Lin 2003; Jacobsson et al. 2004; Koman et al. 2004; Chitra and Nandini 2005; Blair and Watson 2006; Bober and Kobel- Buys 2006; Korzeniewski 2006; Thorngren- Jerneck and Herbst 2006; Öztürk et al. 2007; Robertson et al. 2007; Schaefer 2008; Baxter 2009; Sillier at al. 2010; Wu et al. 2010; Milewska et al. 2011; Reid et al. 2011). This syndrome is the first cause of motor disability and the second cause of neurodevelopmental abnormalities in children after intellectual disability (Michalska et al. 2012).

The polyetiological nature of CP and the pathophysiological mechanisms leading to its formation are not fully understood yet, which is the main reason for the constant search for independent factors predisposing to its occurrence (Sternal et al. 2011).

The aim of the study was to examine the effect of maternal age on the risk of CP development, taking into account all significant risk factors and the division into single, twin, full-term, and pre- term pregnancies.

Methods

Participants

The study included a group of 278 children diagnosed with CP, born in the years 1976–2010, attending public and non-public educational-and-therapeutic institutions in Poland. The tool used in the research was a questionnaire completed by mothers of children with CP or, failing that, by the child's closest caregiver. Data was collected in 40 Polish centers dealing with the care and rehabilitation of children with CP. The control group included data from medical documentation of 435 neonates born without congenital abnormalities, genetic syndromes, metabolic disorders, or other hereditary diseases in the years 1990–2010 in Limanowa County Hospital in the Name of God's Mercy, Poland (Polish: Szpital Powiatowy Imienia Miłosierdzia Bożego in Limanowa).

Data collection

This work is only a fragment of extensive scientific research, the aim of which was to select, among demographic, antenatal, perinatal, and neonatal factors, independent risk factors for the development of CP (Sternal et al. 2020a, 2020b, 2021). Factors influencing pregnancy and childbirth play a significant role in the eti-

ology of CP; therefore, the first part of the questionnaire covered the mother's medical history, family, and obstetric history, as well as questions about childbirth, pregnancy, gynecological disorders, and information about the child's father. The second part of the questionnaire included questions about medical and anthropological information, as well as the prevalence of comorbidities and diseases of the child. The last part of the questionnaire was an environmental diagnosis concerning the structure of the family, place of residence, acquired education, and profession of the child's parents, as well as the mother's financial situation during pregnancy.

Cases of acquired CP, congenital hydrocephalus in the course of genetic syndromes (Arnold-Chiari syndrome, Dandy-Walker syndrome), and congenital microcephaly were excluded from the study. Data on mothers and newborns – information about the parents and the condition of the newborn – were collected on the basis of available medical documentation (hospital treatment information card, nursing care card, midwife-led care card, neonatal card) – information concerning parents and the state of the neonate. The following parameters were evaluated during this study: systemic inflammatory response syndrome (SIRS), elevated CRP level, diagnosed fungal, bacterial, or viral infection or antibiotic therapy.

Study design

In the light of the available literature, the etiology of CP is different in premature and full-term newborns, as well as in singleton and twin newborns. Therefore, for a reliable assessment of the risk of developing CP, the material was divided into groups according to single and twin pregnancies, as well as full-term (≥37 weeks gestation) and pre-term (<37 weeks gestation) pregnancies (Table 1).

The research used the assumption that the main predictors of CP were gestational age (the week of pregnancy termination) and multiplicity of pregnancies (single / twin pregnancy). Accordingly, the entire research procedure was aimed at demonstrating that, depending on different gestational age groups, risk factors for CP are different. Therefore, different models should be created to estimate this risk. The groups distinguished in the material differ significantly in terms of the etiopathogenesis of CP due to single, twin, full-term, and pre- term pregnancies. Therefore, the existence of variables

Table 1. The number of children in the CP and control group in the groups used for analyses

Name of the group	Children with CP		Control group		All children	
	N	%	N	%	N	%
All children	278	39.0	435	61.0	713	100.0
Children from single pregnancies	250	89.9	419	96.3	669	93.8
Children from twin pregnancies	28	10.1	16	3.7	44	6.2
Children from full-term pregnancies	152	54.7	396	91.0	548	76.9
Children from premature pregnancies	126	45.3	39	9.0	165	23.1
Children from full-term, single pregnancies	143	94.1	384	97.0	527	96.2
Children from full-term, twin pregnancies	9	5.9	12	3.0	21	3.8
Children from premature, single pregnancies	107	84.9	35	89.7	142	86.1
Children from premature, twin pregnancies	19	15.1	4	10.3	23	13.9

that differentiate the above-mentioned groups was initially assumed. The scheduled one-dimensional analyses with the use of variables such as birth weight, birth length, gestational age, birth order and sex were aimed at the comparative characteristics of children from the CP and control group in the above-mentioned groups, as well as at the determination of variables that, after inclusion in logistic regression models, served as covariates controlling the proper statistical inference.

Statistical analyses

In order to assess the likelihood of CP occurrence depending on the membership in a designated group and co-occurring covariates, several logistic regression models were planned:

- a simple model that determines the raw odds ratio (OR) of the occurrence of CP due to the factors studied in each of the designated groups,
- an adapted model that considers the impact of the univariate covariates determined in the analyses,
- the complete model, which, in addition to the covariates and significant risk factors, also considers the influence of father's and mother's age (so that the independent influence of mother's and father's age can be assessed depending on the factors studied and group membership).

To reduce the likelihood of a sparse response matrix, the planned research also included the execution of logistic regression models with and without data aggregation. Additionally, taking into account the possibility of skewness of covariates, the research also used a regression model with transformed variables.

In individual logistic regression models, in order to estimate the odds ratio more precisely, the parameterization of the variable was planned with the separation of the reference groups in which the risk of CP was estimated. Two categories of the mother's age variable were used: ≤20 years, 30–34 years, 35–39 years, ≥40 years, reference group: 21–29 years, and ≤24 years, ≥30 years, reference group 25–29 years. The variable categorization in three variants was used in the case of a rarefied response matrix, when the division into 5 age categories could not be applied. In order to assess the independent risk factors of CP, a logistic regression model was planned considering all the demographic, antenatal, perinatal, and neonatal factors important in multivariate analyses, as well as important covariates.

Analyses were performed using STATISTICA 12.5. The comparative characteristics of the group of children with CP and children from the control group were performed using the Mann-Whitney *U* test, Student's *t*-test for independent samples (against groups), and the Chi-square test in the case of nominal variables. Variables that differentiated the groups of children with CP and the control group and were statistically significant in the univariate analyses were included in the principal components analysis. This enabled the isolation of uncorrelated covariates, which were included in further multivariate analyses.

The OR (odds ratio) was calculated to determine the relationship between the studied variables and CP. The OR value was given with the estimation measure in the form of a 95% confidence interval, giving the significance *p*-level for the Wald Chi-square test. The fit of the data was checked using the Pearson

Chi-square statistic, the yaw statistic, the scaled Pearson Chi-square statistic, and the scaled yaw statistic. The model fit measures were also expressed using Cox-Snell and Nagelkerke coefficients, as well as the Hosmer-Lemeshow test.

Results

The one-dimensional analysis showed that in the group of all children and the group of children from single pregnancies, the variables regarding weight, birth length, birth order, and gestational age

Table 2. Comparative characteristics of all children from the study and control groups, and separately for single and twin pregnancies

All children			
Variable	Group of children with CP $N = 278$	Control group $N = 435$	*p*-level
Sex: M/F	152/126	219/216	NS
Birth weight (g)	440.0–5600.0 2554.9±997.2	1290.0–5170.0 3367.1±552.0	<0.001
Birth length (cm)	20–65 50.0±7.2	41–63 54.8±3.1	<0.001
Birth order	1–9 2.0±1.3	1–15 2.6±1.8	<0.001
Gestational age <37 Gestational age ≥37	126 151	39 396	<0.001
Children from single pregnancies			
Variable	Group of children with CP $N = 250$	Control group $N = 419$	*p*-level
Sex: M/F	136/114	217/202	NS
Birth weight (g)	440.0–5600.0 2615.2±1005.6	1430.0–5170.0 3403.87±514.07	<0.001
Birth length (cm)	20–65 50.3±7.12	45–63 54.9±2.9	<0.001
Birth order	1–9 2.0±1.3	1–15 2.6±1.8	<0.001
Gestational age <37 Gestational age ≥37	106 141	35 381	<0.001
Children from twin pregnancies			
Variable	Group of children with CP $N = 28$	Control group $N = 16$	*p*-level
Sex: M/F	16/12	2/14	<0.01
Birth weight (g)	830.0–3750.0 2025.7±745.4	1290.0–3230.0 2403.1±650.4	NS
Birth length (cm)	33–63 47.4±7.0	41–56 49.9±4.4	NS
Birth order	1–4 1.8±1.0	1–5 2.6±1.5	<0.05
Gestational age <37 Gestational age ≥37	20 8	4 12	<0.01

Data were expressed as group size, range of variation or mean and standard deviation, *p*-level from Student's *t*-test, Mann-Whitney *U* test or Chi-square test; NS stands for 'not significant.'

were significantly different in children with CP in comparison with children from the control group. On other hand, in the group of children from twin pregnancies, sex, birth order, and gestational age were significantly different in children with CP compared to the control group (Table 2).

In the group of children from full-term and full-term single pregnancies, the variables of birth weight, birth length, and birth order were significantly different in children with CP from those from the control group. On the other hand, among children from full-term twin pregnancies, the gender and birth order were significantly differentiating factors (Table 3).

In the group of children from pre-term pregnancies and in the group of children from pre-term single pregnancies, the variables: birth weight and birth length were significantly different ini children with CP from those from the control

Table 3. Comparative characteristics of children from full-term, full-term single, and full-term twin pregnancies from the study and control groups

Children from full-term pregnancies			
Variable	Group of children with CP *N* = 152	Control group *N* = 396	*p*-level
Sex: M/F	86/66	203/193	NS
Birth weight (g)	2180.0–5600.0 3307.4±540.3	1480.0–5170.0 3453.3±472.5	<0.01
Birth length (cm)	35–63 54.3±3.9	46–63 55.2±2.7	<0.05
Birth order	1–9 1.9±1.2	1–5 2.6±1.5	<0.001
Children from full-term single pregnancies			
Variable	Group of children with CP *N*= 143	Control group *N*= 384	*p*-level
Sex: M/F	80/63	201/183	NS
Birth weight (g)	2225.0–5600.0 3339.7±529.7	2050.0–5170.0 3479.3±446.3	<0.01
Birth length (cm)	35–63 54.4±3.9	46–63 55.3±2.6	<0.05
Birth order	1–9 1.9±1.2	1–15 2.6±1.8	<0.001
Children from full-term twin pregnancies			
Variable	Group of children with CP *N*= 9	Control group *N*= 12	*p*-level
Sex: M/F	6/3	2/10	<0.05
Birth weight (g)	2180.0–3750.0 2801.1±470.9	1480.0–3230.0 2620.8±548.9	NS
Birth length (cm)	49–63 52.9±4.9	47–56 51.8±2.8	NS
Birth order	1–4 1.8±0.9	1–5 3.2±1.4	<0.05

Data were expressed as group size, range of variation or mean and standard deviation, *p*-level from Student's *t*-test, Mann-Whitney *U* test or Chi-square test; NS stands for 'not significant.

group. However, in the group of children from pre-term twin pregnancies, none of the variables was statistically significant (Table 4).

After the analysis of principal components, based on the absolute values of the factor loadings, birth weight and birth order were included as accompanying variables (controlling proper statistical inference) in the groups of all children, children from single, full-term, and full-term single pregnancies in logistic regression models. On other hand, in the groups of children from pre-term and pre-term single pregnancies only birth weight was included. No covariates were determined for the groups of children from twin pregnancies, full-term twin pregnancies, and pre-term twin pregnancies, as these groups were too small to perform maximum likelihood estimation in the logistic regression models.

The mean age of mothers in the group of children with CP was 27.9 years, and

Table 4. Comparative characteristics of children from pre-term pregnancies, pre-term single pregnancies, and pre-term twin pregnancies from the study and control groups

Children from pre-term pregnancies			
Variable	Group of children with CP *N* = 126	Control group *N* = 39	*P*-level
Sex: M/F	66/60	16/23	NS
Birth weight (g)	440.0–4600.0 1644.9±572.8	1290.0–3580.0 2491.3±499.4	<0.001
Birth length (cm)	20–65 44.5±6.6	41–57 50.2±3.6	<0.001
Birth order	1–9 2.1±1.4	1–7 2.2±1.3	NS
Children from pre-term single pregnancies			
Variable	Group of children with CP *N* = 107	Control group *N* = 35	*P*-level
Sex: M/F	56/51	16/19	NS
Birth weight (g)	440.0–4600.0 1642.4±581.0	1430.0–3580.0 2576.0±485.7	<0.001
Birth length (cm)	20–65 44.5±6.7	45–57 50.8±3.1	<0.001
Birth order	1–9 2.2±1.5	1–7 2.3±1.3	NS
Children from pre-term twin pregnancies			
Variable	Group of children with CP *N* = 19	Control group *N* = 4	*P*-level
Sex: M/F	10/9	0/4	NS
Birth weight (g)	830.0–2360.0 1658.4±540.2	1290.0–2300.0 1750.0±502.1	NS
Birth length (cm)	33–55 44.6±6.4	41–48 44.8±3.8	NS
Birth order	1–4 1.9±1.1	1 1±0	NS

Data are expressed as group size, range of variation or mean and standard deviation, *p*-level from Student's *t*-test, Mann-Whitney *U* test or Chi-square test; NS stands for 'not significant.'

in the control group – 28.2 years. In the group of children with CP, 43.9% of women were primigravidae, and in the control group – 34.5%. On other hand, 7.2% of the mothers of children with CP were ≤20 years old, and 16.2% were ≥35 years old. In the control group, 5.5% of women were ≤20 years old, and 13.7% were ≥35 years old (Fig. 1, Table 5).

Of all the logistic regression models used to estimate the risk of CP for demographic factors (including mother's age), the original data were best reproduced by the models adjusted to covariates (both with and without data aggregation). For all age categories included in the estimated models (assessing the effect of demographic factors on the development of CP), only the category of ≤24 years of age (in the group of all children) was significant. It was estimated that in this mother's age category, the risk of CP is lower (OR 0.6, 95% CI: 0.3–1.0) in comparison to mothers aged 25–29 both in adapted model and in model with aggregation as well (p=0.03) (Table 6). The

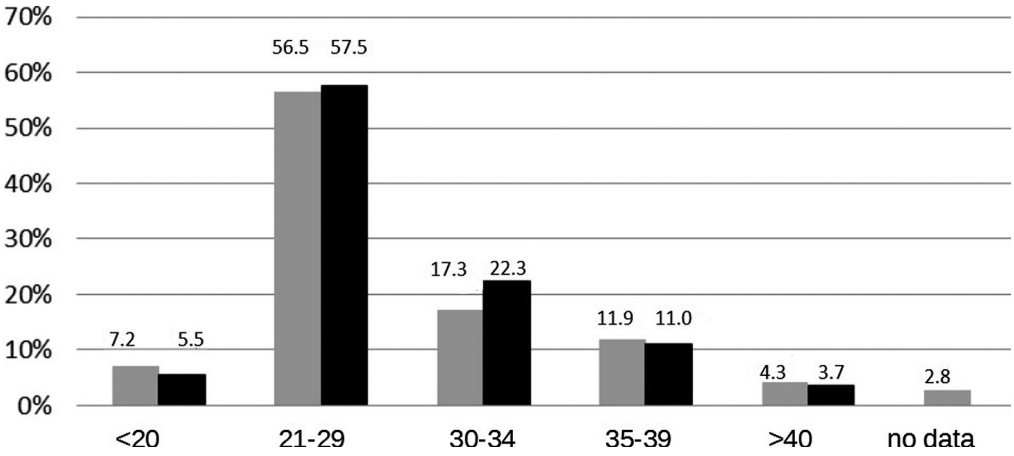

Fig. 1. Age structure of women in labour in the group of children with CP (grey) and in the control group (black)

Table 5. Age of primigravidae, primiparae, and multiparae at birth in the group of children with CP and the control group

Age of primigravidae (years) (p-level NS)						
Group	N	$\bar{x}$	Me	S	Min	Max
Children with CP	122	25.3	25.0	4.9	16.0	40.0
Control group	150	24.3	24.0	3.6	17.0	39.0
Age of primiparae (years) (p-level NS)						
Group	N	$\bar{x}$	Me	S	Min	Max
Children with CP	8	27.5	27.5	4.9	20.0	37.0
Control group	10	26.7	25.0	4.8	22.0	36.0
Age of multiparae (years) (p-level NS)						
Group	N	$\bar{x}$	Me	S	Min	Max
Children with CP	144	30.0	29.0	5.7	19.0	44.0
Control group	275	30.4	3.0	5.4	18.0	43.0

effect of maternal age on the occurrence of CP was also analyzed in the group of children from single, full-term, full-term single, as well as pre-term and pre-term single pregnancies, taking into account other demographic factors. There was no significant effect of mother's age on the occurrence of CP in any of the above-mentioned groups.

Using the constructed logit models, potential independent variables significantly influencing the occurrence of CP were selected. Based on the set of significant variables obtained (among demographic, antenatal, perinatal, and neonatal factors), an estimation was made using the full model (all factors deemed significant and adjusted to covariates) in order to obtain a model predicting the effect of a mother's age on the occurrence of CP in each of the separated groups. After including maternal age in the final model (with the combined analysis of important demographic, antenatal, perinatal, and neonatal factors), no effect of this factor on the appearance of CP was observed including models with and without data aggregation.

Discussion

Maternal age has become one of the most discussed risk factors in maternal-fetal medicine, and its multidimensional impact on the developing fetus and the course of pregnancy has made it one of the main topics of epidemiological research. Maternal age is a factor that influences the risk of birth defects in babies. In mothers aged 25 years, the risk of developing genetic disorders in a child is 1/526, at the age of 30 it is 1/385, at the

Table 6. The influence of maternal age on the risk of CP in the control group

Adapted model		
Age class of mother	Wald test	OR (95% CI)
<20	1.00 (0.43–2.34)	$p = 0.99$ (NS)
30–34	1.59 (0.85–2.99)	$p = 0.14$ (NS)
35–39	1.46 (0.57–3.72)	$p = 0.43$ (NS)
≥40	3.08 (0.78–12.02)	$p = 0.11$ (NS)
21–29 (base/reference group)		
≤24	0.57 (0.34–0.96)	$p = 0.03$
≥30	1.40 (0.75–2.60)	$p = 0.29$ (NS)
25–29 (base/reference group)		
Data with aggregation		
Age class of mother	Wald test	OR (95% CI)
<20	0.99 (0.43–2.29)	$p = 0.99$ (NS)
30–34	1.56 (0.83–2.91)	$p = 0.16$ (NS)
35–39	1.45 (0.57–3.67)	$p = 0.43$ (NS)
≥40	3.03 (0.77–11.90)	$p = 0.11$ (NS)
21–29 (base/reference group)		
≤24	0.57 (0.33–0.93)	$p = 0.03$
≥30	1.36 (0.74–2.52)	$p = 0.35$ (NS)
25–29 (base/reference group)		

age of 35 it is 1/179, and in mothers aged 45 and over, 1/19 of born children have genetic disorders (Johnson at al. 2012).

Epidemiological data clearly indicate that after the age of 35, the ability of their body to recognize embryos with genetic defects is weakened. Their organisms become less sensitive to any genetic abnormalities, compared to young women who, in the event of developmental disorders of the fetus, often experience spontaneous miscarriage at an early stage of pregnancy. This should be associated with the aging of ova, the maturation process which in older women is more likely to develop mutational changes. The decreased quality of oocytes and neuroendocrine changes related to biological aging of the organism have a decisive effect on the gradual decrease of the female reproductive potential with age. Experimental studies also show that the risk of complications increases in both the mother and the child due to maternal age. In women of advanced reproductive age, pathological processes disturbing implantation (endometriosis, chronic inflammation in the minor uterus, uterine fibroids), miscarriages, ectopic pregnancies, placenta previa, gestational diabetes, preeclampsia, increased blood pressure during pregnancy, multiple births, premature births, abnormal fetal position, uterine rupture, or stillbirths are significantly more frequent (Albers et al. 1995; Heffner 2004; Usta and Nassar 2008; Rajaee et al. 2010; Liu and Case 2011; Canterino 2012; Hoque 2012; Karoshi and Newbold 2012; Khalil et al. 2013; Laopaiboon et al. 2014). In the light of the available literature, all these complications may be causally related to the development of CP (Asher and Schonell 1950; Radecka and Chmielińska 1974; Fletcher and Foley 1993; Platt and Pharoah 1995; Spinillo et al. 1998; Blair and Stanley 2002; Thorngren- Jerneck and Herbst 2006; Wu et al. 2010; Milewska et al. 2011; Sternal et al. 2011; Wu et al. 2011; Lang et al. 2012; McIntyre et al. 2013).

It has also been shown that maternal age influences the biological condition of newborns. Newborns of mothers in labour over 35 years of age are biologically weaker, most of them being premature or dystrophic newborns. Complications of delivery and adaptation difficulties in the neonatal period are observed in them more frequently. Undoubtedly, the increased risk of diseases in newborns of older mothers can be explained by the depletion of their biological abilities, mainly due to the correlation of maternal age with the value of produced gametes. In the case of primigravidae, the labour usually lasts longer, and the course of labour itself is more traumatic for the newborn.

Adolescent mothers are associated with reduced birth weight of newborns, which may result from the limited possibilities of the mother which is still developing. Maternal age is also indirectly related to habits, behavior, psychological attitude towards pregnancy, and social position, as well as, undoubtedly, birth order and the sequence of pregnancies. Thus, maternal biological age contains information about the complex of maternal factors, and thus must be understood as a broad concept, and not as a single factor (Radecka and Chmielińska 1974; Cieślik and Waszak 1992; Michałowicz 2001).

The relationship between maternal age and the occurrence of CP is still controversial. Many epidemiological studies have shown a significant correlation between advanced age (over 35 years of age

on average) of the mother and the risk of developing CP (Platt and Pharoah 1995; Michałowiecz 2001; Blair and Stanley 2002; Jacobsson and Hagberg 2004; Thorngren-Jerneck and Herbst 2006; Gilbert et al. 2010; Wu et al. 2010, 2011; McIntyre et al. 2013; Soleinami et al. 2013). There are, however, studies that did not show such a relationship (O'Shea et al. 1998; Gray et al. 2001; Kułak and Sobaniec 2004). The problem of the relationship between adolescent mothers and the occurrence of CP is similarly ambiguous. According to Jacobsson and Hagberg (2004), Michałowicz (2001), Thorngren-Jerneck and Herbst (2006), Wu et al. (2011) and Lang et al. (2012), adolescent mothers (under 19 years of age on average) increases the risk of CP. However, in the opinion of others, young age has no effect on the occurrence of CP (Radecka and Chmielińska 1974; Murphy et. 1995; O'Shea et al. 1998; Wu et al. 2000; Gray et al. 2001; Kułak and Sobaniec 2004). The available literature also includes studies, in which the effect of maternal age on the occurrence of CP was not shown (Milewska et al. 2001; Jacobsson et al. 2002; Grether et al. 2003; Kułak and Sobaniec 2004; Takahashi et al. 2005; Škrablin et al. 2008), which is consistent with our findings.

After including maternal age in the final model (with the combined analysis of important demographic, antenatal, perinatal, and neonatal factors), no effect of this factor on the appearance of CP was observed in our research. When examining the effect of maternal age on the basis of various constructed models in the gestational age groups, it was noticed that the complexity of this factor and the interaction of its various components is the main reason for the unclear image of these relationships or the lack thereof. Further analyses should seek to estimate the influence of maternal age while controlling all the variables that are linked to the general concept of a mother's biological age. As the conducted analyses have shown, it is also important to study the effect of maternal age on the occurrence of CP with the simultaneous control of other demographic factors (father's age and the material status of parents).

Statistical analyses revealed that birth weight and pregnancy sequence are significant covariates that significantly change the values of estimated parameters; therefore, they should be used as controlling variables when trying to assess the risk of CP. Moreover, the multivariate analyses showed that the risk factors for CP differ depending on the type of pregnancy (twin, single, full-time, full-time single, pre-term, and pre-term single pregnancies), and that models estimating the odds ratio of CP should be made in this respect. Further research, including twin, full-term twin, and preterm twin pregnancies, is required to identify all the independent risk factors for the development of CP.

Moreover, a limiting factor in this study should be also mentioned. It was broadly discussed in previous papers concerning the various factors influencing the risk of CP (Sternal et al. 2020a, 2020b, 2021). The authors are aware of the limitations of the retrospective method and further studies, if possible, should be conducted by the prospective method as well. Additionally, the broad time range of this study may have influenced the obtained results because of socioeconomic factors, life quality and development of medicine changed over this time range.

It became apparent that maternal age is a weak predictor of CP, and is insig-

nificant in the final logistic regression model. It seems correct to assume that the studies conducted so far, showing a significant effect of maternal age in this respect, may be associated with bias in the estimators used to assess the risk of CP due to the fact that other important risk factors for CP development were not included in the research.

The Author's contribution

MS conceived the paper, collected the data, performed statistical computations and drafted the manuscript. BK was project supervisor, co-edited the final version of the manuscript. KB performed statistical computations and co-edited the final version of the manuscript. AT performed statistical computations, drafted the manuscript, co-edited the final version of the manuscript. All authors carefully read and accepted the final version of the manuscript.

Conflict of interest

The authors declare that there is no conflict of interest.

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