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APPEARANCE OF NEURODEVELOPMENTAL DISORDERS IN CHILDREN DELIVERED POST-TERM: A CROSS-SECTION STUDY

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ABSTRACT

Goal: To analyze the appearance of neurodevelopmental disorders in children delivered post-term and to find out whether prolonged pregnancy may be a cause of such disorders in a selected group participants. **Patients and methods:** This study included a cohort of 34 children born post-term suffering from neurodevelopmental disorders who were treated at the Service for psycho-physiological and speaking disorders in Mostar, Bosnia and Herzegovina during an 18-year period. **Results:** There were 59.4% of male and 40.6% female patients ($P=0.002$). The most common neurodevelopmental disorder in the sample was intellectual disability (38.2%), followed by epilepsy (26.4%), delayed psychomotor development (14.7%), and cerebral palsy (11.7%) ($P<0.001$). The correlation between mothers' parity and post-term delivery was found ($P=0.016$). **Conclusion:** Post-term delivery may be the cause of neurodevelopmental disorders. The most common disorder among them were intellectual difficulties.

Key words: post-term delivery, neurodevelopmental disorders.

1. INTRODUCTION

Post-term pregnancy (gravidity of prolongation) is a pregnancy that lasts more than 42 weeks (294 days), counting from the first day of the last menstrual period (1, 2). Prolonged pregnancy occurs in 7% of all pregnancies, while only about 25% of such pregnancies represent the real threat to the fetus (3). Post-term pregnancy stands for roughly about 10% (between 3.5% and 13.5%) of all pregnancies and it is increased in nulliparous women, as well as in those giving birth to male infants (3-5). It is associated with an increased risk of intrapartum and postpartum obstetric complications and with a high rate of perinatal morbidity and mortality (6, 7). Investigating a possible genetic component to prolonged gestation Laursen et al. established that maternal genetic factors may influence the rate of post-term pregnancy in as many as 30% of cases in their series of 2 588 same-sex twin pairs of whom both co-twins became parents during the period between 1978 and 1996 (8). Another described risk

factor appears to be maternal obesity, which may notably increase the risk of prolonged pregnancy (9-11). Therefore, a high body mass index (BMI) during the first quarter, as well as notable BMI increase during the entire pregnancy are associated with longer gestation and increased risk of post-term pregnancy (9). Contrary, low pregravid BMI may be associated with an increase in the prevalence of preterm delivery (12). In prolonged pregnancy a newborn is at risk due to placental insufficiency, because the placenta develops subacute failure due to its degenerative changes and aging, which results in a decrease of oxygen supply and nutrients to the fetus causing hypoxia, hypoglycemia and dysmaturity (13). During post-term birth there is a higher incidence of fetal distress and appearance of meconic amniotic fluid (14). Therefore, perinatal mortality is four-time higher compared to regular pregnancy (15-18). Prolonged pregnancy is also associated with smoking, the higher risk of macrosomia, and caesarean section, all of which increases the incidence

of neurological disorders (15, 18, 19). Other causes include neonatal injury and newborn overweight (>4500 grams) (20, 21). The lack of cervix maturity occurring in prolonged pregnancies may be due to prostaglandin dysfunction/neurohormonal dysregulation (22, 23). The most common complication attributed to post-term pregnancy is a result of spinal cord compression due to reduction of amniotic fluid (24, 25). Such a pregnancy is an independent risk factor for neonatal encephalopathy too (26). Latest studies also demonstrated that the risks to the fetus (27-39) and to the mother (36-46) of continuing the pregnancy beyond the estimated date of delivery is far greater than expected. Prolonged pregnancy is an indication for enhanced monitoring which includes cardiotocography, load test, biophysical profile, and assessment of amniotic fluid, amnioscopic review or a combination of these methods. However, there is no evidence that one of the methods is more reliable than the other (47).

Classification of developmental disorders recommended by the World Health Organization (WHO) is based on three assumptions: impairment, disability in everyday activities, and handicap (48). According to health and social care regulations of the Federation of Bosnia and Herzegovina, the following disability groups are established: a) visual impairment; b) hearing impairment; c) disorders of speech and voice communication; d) physical disability; e) intellectual disabilities; f) behavioral disorders due to organic disease or psychosis; g) the combination of several types and degrees of disability.

The aim of this study was to investigate the relationship between prolonged pregnancy and developmental disabilities in post-term newborns. We hypothesized that such disabilities may be influenced by prolonged pregnancy.

We believe that this work may move forward the research of this matter, since it is a cross-sectional study conducted during the 18-year period, dealing with various multiple risk factors not entirely and systematically addressed in previous studies.

2. METHODS

A cross-sectional study of neurodevelopmental disorders in post-term newborns was conducted at the Department of psychophysiological and speech disorders, Health Center Mostar, Bosnia and Herzegovina, during the 18-year period.

The criteria of inclusion in the study were: prolonged pregnancy (>42 weeks of gestation), the existence of neurodevelopmental disorders (cerebral palsy, epilepsy, intellectual disability, autism, Down syndrome, West syndrome, hearing impairment, hyperactivity disorders, delayed psychomotor development). The investigated parameters were: the newborn gender, the type and frequency of neurodevelopmental disorders, the parity of mother, etiological factors influencing post-term delivery, speech and language difficulties in post-term children, the type of school program for post-term children, and education level of post-term children's mothers.

The outcome was assessed at the period between 5.5 and 6.5 years post delivery. A Chi-square test was used to compare the frequency in differences of nominal variables between groups. A p value <0.05 was considered statistically significant. A software system SPSS for Windows (version 13.0, SPSS Inc., Chicago, Illinois, USA) and Microsoft Excel

(version Office 2003, Microsoft, Redmond, WA, USA) was used for the statistical analysis.

3. RESULTS

A cohort of 34 post-term newborns was analyzed. There were 21 (59.4%) boys and 13 (40.6%) newborn girls in the sample. Investigating the type and incidence of neurodevelopmental disorder in post-term newborns the following was found: intellectual disabilities were recorded in 13 out of 34 (38.2%) newborns, followed by epilepsy in 9 (26.4%), delayed psychomotor development in 5 (14.7%), cerebral palsy in 4 (11.7%), and Down syndrome in 3 (8.8%) The difference was statistically significant ($\chi^2=10.118$; $p=0.038$). (Figure 1). Considering the parity of mother in post-term pregnancy it was observed that there were 24 (70.6%) multiparas women and 10 (29.4%) primipara in the investigated sample. The difference was statistically significant ($\chi^2=5.765$; $p=0.016$). (Table 1).

Considering the etiological factors influencing post-term delivery, in 16 out of 34 (47%) newborns no known causative factors were found. Asphyxia and hypoxia were found in 11 (32.3%), hypoxic-ischemic brain damage in 5 (14.7%), intrauterine complication in 2 (5.8%), and chromosomopathy in one (2.9%) participant (Figure 2). The difference among the groups was statistically significant ($\chi^2=19.607$; $p=0.000$).

Considering the speech and language difficulties registered in post-term children, neat speech was recorded in 10 out of 34 (29.4%), underdeveloped speech in 8 (23.5%),

| Variable | N (%) | χ^2 test | p |
|-------------|------------|---------------|-------|
| Parity | | 5.765 | 0.016 |
| Primipara | 10 (29.41) | | |
| Multiparous | 24 (70.59) | | |

Table 1. The parity of mother in post-term pregnancy

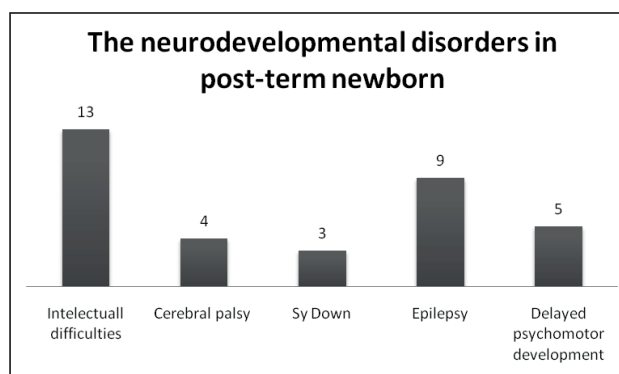


Figure 1. Overview of the neurodevelopmental disorder type in post-term newborns

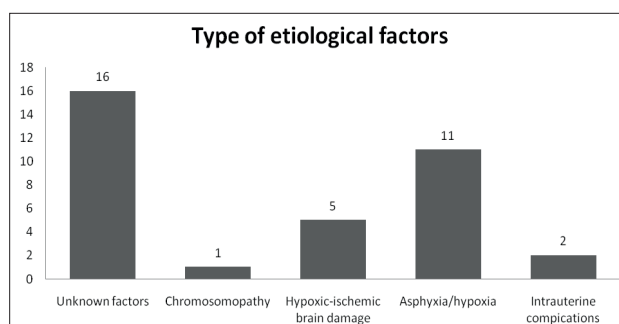


Figure 2. Etiological factors influencing post-term delivery

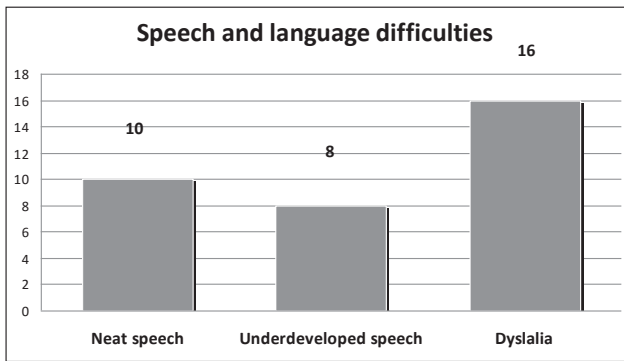


Figure 3. Speech and language difficulties in post-term children

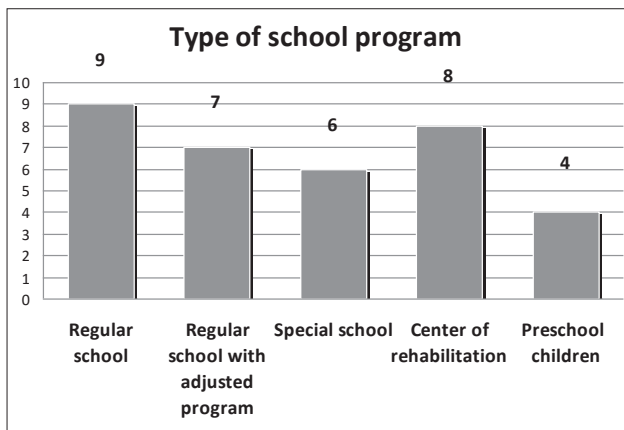


Figure 4. Type of school program for post-term children

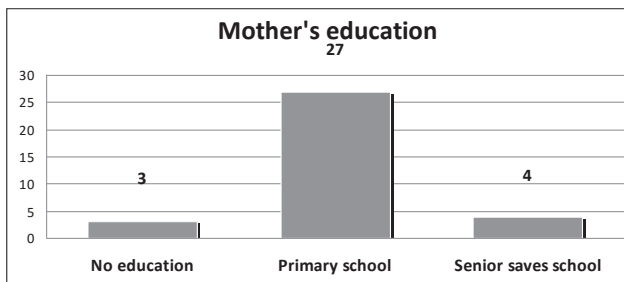


Figure 5. Education level of post-term children's mothers

and dyslalia in 16 (47.1%) children (Figure 3). The difference among the groups was statistically significant ($\chi^2=19.607$; $p=0.000$).

Considering the type of school program for post-term children, regular school was attended by 9 out of 34 (26.5%), regular school with adjusted program by 7 (20.6%), special school by 6 (17.6%) children, while 8 (23.5%) of them were received in center for rehabilitation. There were also 4 (11.8%) preschool children in the investigated sample (Figure 4). The difference among the groups was not statistically significant ($\chi^2=1.301$; $p=0.861$).

Considering the education level of post-term children's mothers, 3 out of 34 (8.8%) mothers had no education, 27 (79.4%) completed primary school, and 4 (11.8%) of them senior saves school (Figure 5). The difference among the groups was statistically significant ($\chi^2=29.831$; $p=0.000$).

4. DISCUSSION

Reviewing the literature we found out that rather small number of studies has attributed the risk factors for neurodevelopment disorders to post-term delivery.

In this study, we analyzed the influence of gender, the type and frequency of neurodevelopmental disorders, the mother's parity, etiological factors as a risk of neurodevelopmental disorders in prolonged pregnancy, speech and language difficulties in post-term children, the type of school program such children were enrolled, and education level of post-term children's mothers, speculating that everything mentioned above may be a possible consequence of prolonged pregnancy.

A higher incidence of boys with neurodevelopmental disorders was found, which was similar to the results of other studies (4). Gould et al. stated that the prevalence of all-cause childhood disability is higher among boys than girls in the early years, although by late teens the prevalence rate among girls is similar to that of boys (48).

Intellectual difficulties, epilepsy, cerebral palsy, and delayed psychomotor development were all recorded in our series. The most common neurodevelopmental disorder in our sample was the one concerning intellectual difficulties, followed by epilepsy and cerebral palsy. The difference between the group with cognitive difficulties and other investigated groups was statistically significant ($p=0.038$) (Figure 2).

According to the results of our study, epilepsy and cerebral palsy both had a higher frequency in prolonged pregnancy, while post-term delivery was a risk factor for encephalopathy (hypoxic-ischemic brain) damage. Our results are in accordance with other researches investigating the same matter (49-52). Lindström et al. reported the similar results finding that the post-term delivered children had more developmental disorders such as cerebral palsy, learning difficulties, difficulties in social interaction, especially those aged between 4 and 5.5 years (53).

We analyzed the relationship between maternal parity and prolonged pregnancy. Some studies have shown a higher incidence of post-term delivery in primipara (54), whereas in our sample prolonged pregnancies were mostly found in multiparous women. The difference between the groups was statistically significant ($\chi^2=5.765$; $p=0.016$) (Table 1).

Considering the etiological factors influencing post-term neurodevelopmental disorders, most risk factors remained unknown. Among those of known cause most frequent were asphyxia/hypoxia and cerebral hypoxia/ischemia (hypoxic ischemic encephalopathy) due to perinatal or early neonatal complications (Figure 3). Instead of hypoxic ischemic encephalopathy, the preferred term today is neonatal encephalopathy which may be caused by a restriction of intrauterine growth, preeclampsia and an acute intrapartum event, as well as febrile status, maternal infection and thyroid dysfunction (47, 48). Such encephalopathy may be also caused by uteroplacental insufficiency when a suboptimal placenta offers fewer nutrients and less oxygen than a full term fetus requires, which may predispose abnormal fetal development leading to abnormal emotional and behavioral development later (55-57).

In concern to the speech and language difficulties registered in post-term children, all of them had some form of difficulties with a marked predominance of dyslalia in our series (Figure 3). The difference was statistically significant. Disorders of speech and language arise out of a complex

interaction of genetic, environmental, and neural factors. Remembering this, we speculated that one possible risk factor for such disorders may be post-term delivery. It is observed that approximately 6% of children have speech and language difficulties of which the majority will not have any other significant developmental difficulties (58).

In regard to the type of school program which post-term children attended, the majority of them were enrolled on regular school or regular school with adjusted program, while only a small portion of the sample was received in center for rehabilitation. Since the outcome was assessed in the period between 5.5 and 6.5 years post delivery, preschool children were seldom registered in the investigated sample (Figure 4). However, the difference among the groups was not statistically significant.

Investigating the relationship between functional disability and school activity limitations in a study of 41 300 school-age children Msall et al. find out that among children with multiple functional disabilities 29.9% had neurodevelopmental disorders, 27.1% had learning-behavior disorders, and 18.1% had physical disorders, while among those requiring special education, physical disorders accounted for 9.4%, neurodevelopmental disorders for 16.7%, and learning-behavior disorders for 17% (59).

Considering the education level of post-term children's mothers, it is important to stress that overwhelming majority of them in our series had no education at all (79.4%) (Figure 5). Having in mind this, it remains to be seen what the role of mothers' level of education is in the existence of post-term children neurodevelopmental disorders.

Investigating the structure of social disparities in education, Filmer underlined that the low education of mothers may affect family educational decisions in particular, while Currie and Moretti find out a positive relationship between mother's education and child birth weight, which is a strong predictor of child health (60). Similar to other studies, the credibility of our results depends on determining the exact date of birth, and strict defining the term of delivery to decrease the incidence of prolonged pregnancies. Compared to other studies, our results indicate more neurodevelopmental than motor and cognitive deviation.

Considering this, it is extremely important for future studies to meticulously follow all children delivered post-term, as well as to register their neurological development.

The original finding in this study is the fact that the most common disorder appearing in prolonged pregnancy may be an intellectual disability usually caused by hypoxic-ischemic brain damage. A significant percentage of children having such disabilities are harboring the speech and language difficulties too. Therefore, mothers' higher level of education may be noteworthy in diminishing such difficulties in order to facilitate regular school programs attending for their children. Considering this, we would like to stress that there is a strong correlation between the prolonged pregnancy and mothers' low education level which may also contribute to the speech and language difficulties usually noted in such children. It is a vicious circle, since poorly educated mothers are commonly not concerned enough with the possible consequences of post-term delivery and also not competent enough to adequately participate in trying to resolve the

speech and language problems frequently spotted in post-term children.

Finally, we would like to underline some limitation of this study stemming from its retrospective character and relatively small number of participants involved. Therefore, further research on a broader sample is needed to support our findings.

5. CONCLUSION

Due to the increased neurodevelopmental risk to children who are born post-term, each pregnancy lasting 40 weeks or longer should be monitored with full attention and considered as high risk.

Neurodevelopmental disorders are more common in post-term boys. It seems that the most common known disorder is intellectual disability, while the frequently observed etiologic factor is hypoxic-ischemic brain damage.

It seems that the speech and language difficulties are a major consequence of post-term neurodevelopmental disorders. However, most of such children may successfully attend regular school programs.

It is also important to stress the role of mothers' level of education that is related to the existence and grade of post-term children neurodevelopmental disorders.

Monitoring prolonged pregnancy is a complicated and demanding task carrying a risk to the child's health. Therefore, the decision on whether and when to induce delivery is extremely important for fetal survival.

- Author's contribution: all authors contributed equally in the preparation of the manuscript.
- Conflict of interest: none declared.

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