IRSTI 76.29.47: https://doi.org/10.26577/IAM.2020.v1.i2.04

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ROLE OF VARIOUS RISK FACTORS IN THE DEVELOPMENT OF INFANTILE CEREBRAL PALSY

The purpose of this study was to establish the role of various risk factors in the development of cerebral palsy in children, through a retrospective study of 150 children with cerebral palsy (main group) and 150 healthy children (control group). The vast majority of children 88,0% had varying degree psychological and speech delay. 50.7% of children in the control group were found to have had respiratory infections up to 6 times a year. 95.3% of children with cerebral palsy were sick up to 6 times a year. No children were found to be incidentally ill in the main group vs. 43.3% of such children in the control group. The following factors were found to contribute to the development of infantile cerebral palsy syndrome: hyperbilirubinemia, 33.8%, head and cervical spine injuries, 15.2%, severe infections with septic condition, 11.7% of cases. The identification of risk factors is also very important in the early rehabilitation of children at high risk of developing cerebral palsy.

Keywords: children's cerebral palsy, risk factors, postnatal risk factors.

Introduction

The rapidly growing disability is now one of the top challenges faced by modern society and one of the most common causes of lifelong disability [1,2].

Data from the National Genetic Registry of the Republic of Kazakhstan suggest that 2000 to 3500 children are born annually in the country with congenital and hereditary disorders, that is 20.0-24.3 per 1000 live births [3]. Infantile cerebral palsy (CP) accounts for the largest proportion in pediatric disability profile: 30% to 70%. In Kazakhstan, according to statistics, there are registered more than 44 thousand disabled children, of which number over 10 thousand are diagnosed with cerebral palsy [3].

In Kazakhstan the prevalence of cerebral palsy has increased 1.6 times from 44.6 in 2006 to 73.6 in 2015 per 100,000 population [3].

Children suffering from infantile cerebral palsy require constant care, long courses of expensive comprehensive therapy both inpatient, and outpatient. Most such children are socially maladapted and dependent on others [4]. Development of adaptation, socialization and employment programs, the earliest possible introduction of new therapeutic modalities to intensify the rehabilitation activities in cerebral palsy with a decrease in the number of adverse outcomes, such as disability, are strategic focus areas for health care authorities dealing with this problem [5].

Material and Methods

The study we conducted was designed as a retrospective analytical research into the risk factors for cerebral palsy development in 150 children in the city of Almaty, by reviewing the following primary medical records of recruited participants and their mothers: a record of discharge from a maternity hospital (Form No. 113/u), newborn development record (Form No. 097/u), delivery record (Form 096/u), prenatal/notification record or individual card of a pregnant woman (Form 111/u), child development record (Form 112/u), case report (Form 027/u) [6].

The study was approved by the KazMUCE Local Ethical Committee. Informed consent was obtained from parents or guardians of the children.

A control group comprising 150 healthy children of the same age, homogenic in terms of age and gender, was set up to obtain a reliable assessment of the results.

The control group children were recruited from the catchment areas of pediatric polyclinics in Almaty, with the informed consent of parents/guardians of the children secured.

For data input, we used the MS Access program based on DBMS (Database Management System). The materials entered into the database were processed using modern methods of variation statistics and SPSS software (version 20.0).

Continuous quantitative variables are presented as mean values with standard deviation (±SD) in case of normal data distribution or as median and quartiles. Category variables are presented as numbers and proportions.

Primary statistical processing of data was carried out to determine the prevalence (as percentage) of CP risk factors for the case group as a whole, then by clinical diagnoses and time of CP onset. Average relative values (percentages) with the value of their standard error were obtained. The Student t-criterion (for quantitative variables with normal distribution) was used to compare the data for subgroups. The differences were considered statistically significant if p values were less than 0.05. To see if there were correlation dependence between studied attributes and relationship between factorial and effective attributes we calculated Pearson's linear correlation coefficient (r).

When studying the relationship between nominal variables, in cases where the number of 'expected frequency less than 5' cells in the analyzed table exceeded 25%, the Likelihood Ratio test (LR) was used, the differences were considered statistically significant if $p < 0.05$.

Based on the results of this research, working hypotheses on statistically significant cerebral palsy risk factors have been developed using formal logic methods. These hypotheses will warrant the design of subsequent analytical studies to see if they are useful to substantiate the prospective planning of measures to prevent the cerebral palsy development.

Results and Discussion

Of 150 children with cerebral palsy aged 6 months to 18 years at the time of the study, 95 (63.3%) were boys and 55 (36.7%) were girls.

The age profile showed dominance of primary and secondary school age children, 8 to 12 years (46.2%). One third of the children were preschoolers, 3 to 7 years of age (33.1%); 17.9% were 13 to 17 years, 1.4% 6 months to 2 years and 1.4% under 6 months of age.

43.4% of children were diagnosed with cerebral palsy after the first year of life, 32.4% at 7 to 12 months, and 24.1% at 3 to 6 months of age.

In each case, the clinical type was verified against the ICD-10.

Figure 1 shows the breakdown of various clinical types of cerebral palsy in children under the study.

As seen from Fig.1, dominating among clinical types of cerebral palsy was spastic diplegia, diagnosed in 33.8% of children. 23.4% of children were diagnosed with mixed form of cerebral palsy, less frequently diagnosed were hemiplegic (15.2%), dyskinetic (14.5%) and atonic (11%) types of cerebral palsy. In 3 cases (2.1%), the outpatient records failed to indicate the type of cerebral palsy.

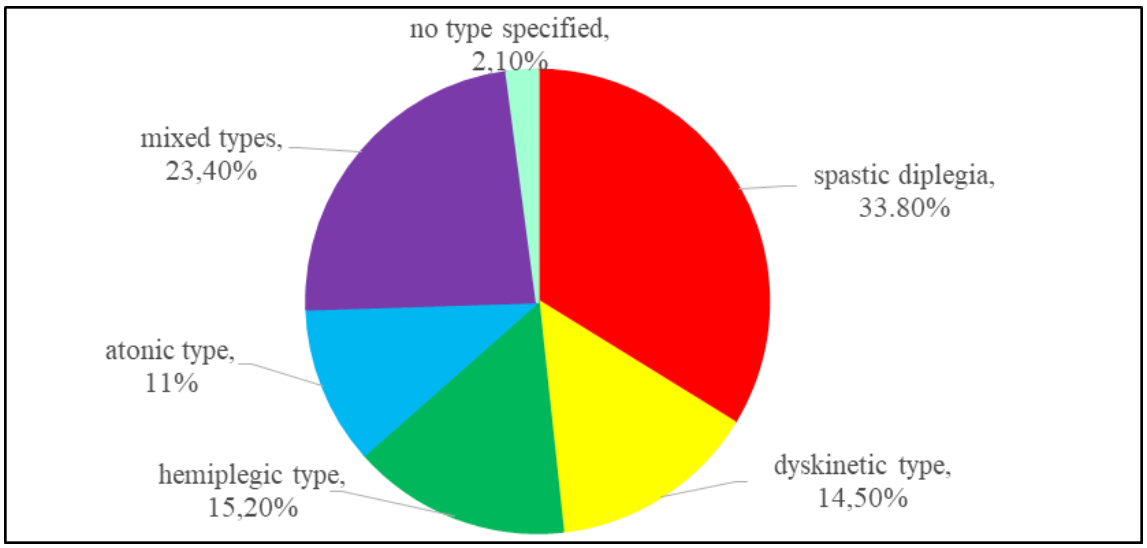

Figure 1 – Distribution of CP types in children (compiled by the author)

Table 1 - Infant feeding practices under 6 months of age

	Main group		Control group		Total	
	abs. number	% of Total, $X \pm \varsigma_x$	abs. number	% of Total, $X \pm \varsigma_x$	abs. number	% of Total, $X \pm \varsigma_x$
Breastfeeding	60	40±4.0	134	89.3±2.5*	194	64.7±2.9
Mixed	21	14.0±2.8	0	0	21	7±1.6
Artificial	34	22.7±3.4	0	0	34	11.3±2.0
No response	35	23.3±3.5	16	10.7±2.5*	51	17±2.3
Total	150	100±0.0	150	100±0.0	300	100±0.0

Note: * the differences between the main and control groups are statistically significant

Breast milk is the best diet for infants, as it provides all nutrients to a baby. Table 1 shows that only 40% of CP children were exclusively breastfed vs. 89.3% of those in the control group. In the main group, 14% were on the mixed feeding and 22.7 % of children were artificially fed.

Children with cerebral palsy were found to have comorbidities (Table 2). The vast majority of children (88.%) had varying degree psychological and speech delay.

Table 2 – Comorbidities in CP children

Comorbidity	Abs.nmber	%
Psychological and speech delay	128	88,3
Visual and hearing impairments	93	64,1
Bone and joint disorders (scoliosis, deformities)	88	60,7
Encephalopathy	78	53,8
Hydrocephalus	73	50,3
Pneumonia	63	43,4
Symptomatic epilepsy	45	31,0
Pseudobulbar disorders	34	23,4
CNS birth defects	31	21,4
Microcephaly	27	18,6
Acute stroke sequelae	23	15,9
Febrile seizures	14	9,7
Sequelae of meningoencephalitis	11	7,6
Osteomyelitis	10	6,9
Down syndrome	4	2,8
Mild mental retardation (oligophrenia)	4	2,8

More than half of the children had visual and hearing abnormalities (64.1%) and bone and joint disorders (60.7%). Half of the children had encephalopathy (53.8%) and hydrocephalus (50.3%). One in three children was diagnosed with symptomatic epilepsy (31.0%), pseudobulbar

disorders (23.4%), and CNS birth defects (21.4%) (as manifested by microcephaly, 18.6%). Notably, nearly half of the children in the study group had the history of pneumonia (43.4%). Pneumonia was more frequently recorded under the age of 1 year: 2 or 3 times a year, with 10% of children having up to 7 relapses annually.

In cerebral palsy, motor and speech disorders are known to be certainly interrelated as demonstrated by the commonality of skeletal and speech musculature disorders [7]. This is due to the damage caused to the motor cortical structures regulating voluntary movements, speech and other cortical functions. To this end, we studied the level of speech development in children with cerebral palsy. Ninety-six per cent of children were found to have a speech development level below age. Speech development disorders were manifested by general underdevelopment of speech, dysarthria, speech delay, alalia.

Table 3 - Intellectual development level of children with cerebral palsy

	Main group		Control group		Total	
	abs. number	% of Total, $X\pm\varsigma_x$	abs. number	% of Total, $X\pm\varsigma_x$	abs. number	% of Total, $X\pm\varsigma_x$
Up to age	0	0	88	58.7±4.0	88	29.3±2.8
Behind age	138	92.0±2.2	62	41.3±4.0	200	66.7±2.9
No verbal contact	6	4±1.6	0	0	6	2±0.9
No response	6	4±1.6	0	0	6	2±0.9
Total	150	100±0.0	150	100±0.0	300	100±0,0

Note: * the differences between the main and control groups are statistically significant

Table 3 shows that the CP children have overwhelmmingly larger percentage of delayed intellectual development compared to the control group ($p<0.05$), with no single instance of up-to-age intellectual development level in the study group. The main and control groups were studied for the incidence of acute respiratory infections (ARI).

Table 4- Incidence of common cold in children

	Main group		Control group		Total	
	abs. number	% of Total, $X\pm\varsigma_x$	abs. number	% of Total, $X\pm\varsigma_x$	abs. number	% of Total, $X\pm\varsigma_x$
< 6 times a year	143	95.3±1.7	76	50.7±4.1*	219	73±2.7
> 6 times a year	6	4±1.6	6	4±1.6	12	4±1.2
Incidentally sick children	0	0	65	43.3±4.0*	65	21.7±2.5
No response	1	0.7±0.7	0	0	0	0.3±0.3
Total	150	100±0.0	150	100±0.0	300	100±0.0

Note: * the differences between the main and control groups are statistically significant

50.7% of children in the control group were found to have had respiratory infections up to 6 times a year. 95.3% of children with cerebral palsy were sick up to 6 times a year. No children were found to

be incidentally ill in the main group vs. 43.3% of such children in the control group (Table 4). Higher ARI incidence in CP children is the result of compromised adaptive capacity, primarily due to organic damage to the regulatory structures of the central nervous system, such as the hypothalamus, hippocampus, cortex.

Figure 2 shows the incidence of postnatal risk factors for cerebral palsy development in the study group.

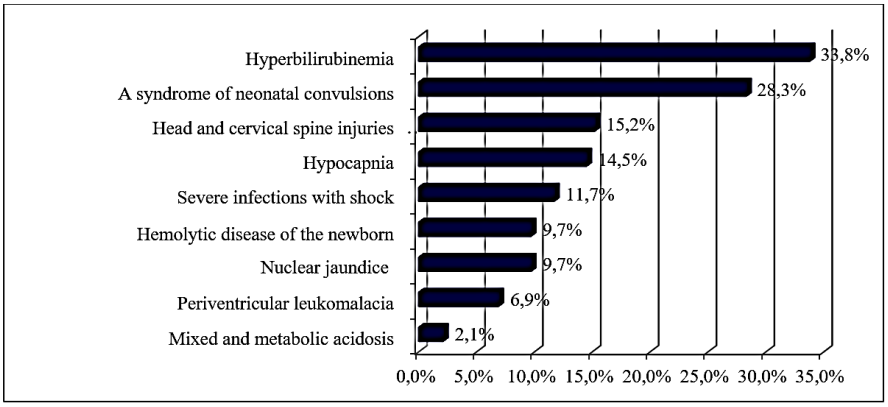

Figure 2 - Postnatal risk factors for cerebral palsy in children (composed by the author)

Among postnatal risk factors, hyperbilirubinemia was detected in 33.8% of cases.

High bilirubin concentration can damage and even destroy the subcortical structures with resultant nuclear jaundice. Nuclear jaundice is an irreversible damage to the central nervous system [8]. In our study, nuclear jaundice occurred in 9.7% of cases.

Hemolytic disease of the newborn was found in 9.7% of cases. Cervical spine injuries are an important factor in the development of cerebral palsy. Injuries to the cervical spine in newborns were found in 15.2% of cases.

In many cases, intrauterine infection was found to have a direct damaging effect on the brain with resultant severe disability of the child. Of particu- lar importance is the TORCH infection group: congenital rubella, cytomegalovirus, toxoplasmosis, herpes. Microorganisms in TORCH-associated intrauterine infections and in exacerbation of chronic reproductive tract infections have a high degree of affinity to nerve cells, leading to the development of intrauterine fetal malformations, and are one of the causative factors for cerebral palsy [9][10]. Se- vere septic infections were reported in newborns in 11.7% of cases.

We researched if there were other children with special needs in families raising children with cerebral palsy. The data is summarized in Figure 3.

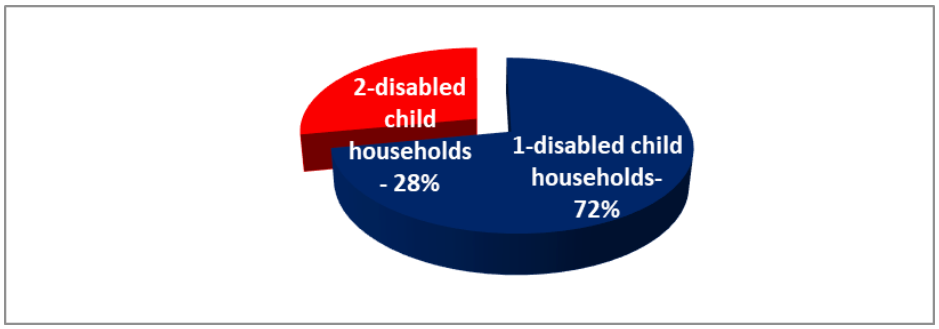

Figure 3 - Number of children with special needs in CP households (compiled by the author)

Twenty-eight per cent of families were found to bring up another child with an established disability, which apart from being an extra financial burden on the family, would have negative impact on the moral and psychological aspect of a family life[11,12,13]. We reviewed the medical records and found 33.0% of children diagnosed with CP within 6 months after vaccination, 13.2% within 7.5 to 12 months, 36.2% within 1 to 2 years and 8.8% within 2 to 3 years after vaccination (Table 5).

Table 5 - Vaccine reactions in the main and control group children

	Main Group		Control group		Total	
	abs. number	% of Total	abs. number	% of Total	abs. number	% of Total
Yes	0	0	62	41.3±4.0*	62	20.7±2.5
No	144	96.0±1.6	88	58.7±4.0*	232	77.3±2.6
No response	6	4±1.6	0	0	6	2±0.9
Total	150	100±0.0	150	100±0.0	300	100±0.0

Note: * the differences between the main and control groups are statistically significant

Review of vaccination status showed that 41.3% of children in the control group had vaccine reactions manifested as fever, ailment, which re- solved in 2 or 3 days. There were no vaccine reac- tions in the main group.

The history data collected and correlation anal- ysis conducted between the various risk factors and the CP type, revealed the following relationships:

- statistically significant relationship between the frequency of pseudo-bulbar disorders and the CP type (likelihood ratio (LR) test, p=0.041), pseu- do-bulbar disorders were more frequent in spastic diplegia);
- statistically significant relationship between epilepsy prevalence and the CP type (LR test, p=0.017), epilepsy was more frequently associated with the hemiplegic type and the unspecified type of cerebral palsy;
- statistically significant relationship between the frequency of encephalopathy and the CP type (LR test, p=0.030), encephalopathy was less fre- quently seen in the hemiplegic form of CP);

statistically significant association between microcephaly and the CP type (LR test, p=0.021), microcephaly was less frequently seen in the dys- kinetic CP and was not observed in the hemiplegic form.

Conclusion

The array of signs and symptoms seen in infan- tile cerebral palsy are provoked by the following postnatal factors: hyperbilirubinemia, 33.8%; head and cervical spine injuries, 15.2%; severe infec- tions with overt sepsis, 11.7% of cases.

In general, the prognosis of social adaptation of CP patients largely depends on how timely the medical, pedagogical and social assistance is ren- dered to the child and his family. Social depriva- tion and inaccessibility of comprehensive care may have a negative impact on the development of a child with cerebral palsy, perhaps even more pro- nounced than the initial structural damage to the brain [14,15].

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