

Changing views of cerebral palsy over 35 years: the experience of a center

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In this study, it was aimed to evaluate the demographic and clinical characteristics of cerebral palsy (CP) cases over a 35-year period. Findings of 442 patients with CP followed from 1995 to 2006 (Group 2) were compared with 208 patients with CP followed between 1972 and 1994 (Group 1) in the same pediatric neurology division. Ratios of both prematurity (38% vs. 17.7%) and very low birth weight (VLBW) infants (13.8% vs. 1.5%) significantly increased in Group 2. There was also a four-fold increase in cesarean delivery in Group 2 (42.3% vs. 9.6%). A significant increase in the rate of early diagnosis during the first year was also found in this group (56.9% vs. 39.4%). The rate of spastic diparesis cases has significantly increased (33.7% vs. 7.7%), while the rate of spastic tetraparesis cases has significantly decreased (63.5% vs. 37.3%). It was seen that preventable risk factors continue today.

Key words: cerebral palsy, etiology, spasticity, tetraparesis, diparesis.

Cerebral palsy (CP) is a disorder of motor function and posture secondary to lesions or anomalies of the immature brain; it is nonprogressive but often changes over time. Children with CP often have other problems such as mental retardation, behavioral disorders, sensorial deficits, epilepsy, and nutritional problems¹⁻³. The worldwide prevalence of CP is approximately 2-2.5 per 1000 live births^{2,4-6}. In Turkey, its prevalence is 4.4 per 1000 live births⁷. In developing countries, perinatal asphyxia, low birth weight (LBW), prematurity, postnatal cerebral infections, and kernicterus are the most common etiological factors⁸. In this study, the data of CP cases (n=442) followed between 1995 and 2006 were compared to the data of CP cases (n=208) followed between 1972 and 1994⁹ at Ege University Faculty of Medicine, Pediatrics Department, Pediatric Neurology Division.

Material and Methods

In this study, 208 patients with CP followed between 1972 and 1994 and previously reported were evaluated as Group 1. Four hundred and

forty-two patients with CP followed between 1995 and 2006 were evaluated as Group 2. The classification of CP was performed according to posture, movement and motor dysfunction¹. Cases were classified as spastic type (tetraparesis: muscle tone increased in all but mainly on upper extremities, diparesis: muscle tone increased in all but mainly lower extremities, hemiparesis: muscle tone increased in one half of the body), ataxic type, which has prominent balance and coordination disorder, and dyskinetic type, which has prominent extrapyramidal findings. The patients who were previously grouped as mixed type (spastic and dyskinetic type) were reclassified according to the predominant clinical findings.

Birth information of the patients was obtained from neonatal data or verbal history. The patients were classified according to their gestational ages: Preterm: gestational age below 38 weeks, Term: gestational age between 38-42 weeks, and Postterm: gestational age over 42 weeks. Birth weight below 1500 g and between 1500-2499 g were accepted as very low birth weight (VLBW) and LBW, respectively.

The etiological classification was based on given clinical criteria combined with available neuroimaging information. Accordingly, etiologic risk factors were determined as prenatally (from conception to the onset of labor), perinatally (from the onset of labor to 28th postnatal day), and postnatally (from 29th day to 2 years of age). Intrauterine infections, central nervous system (CNS) malformation, chromosomal abnormalities, placental insufficiency, maternal chronic disorders, and substance exposure were considered as prenatal risk factors. Prematurity, delivery complications (premature rupture of membranes, placenta previa, abruptio placenta, cord entanglement, fetal distress, prolonged labor, assisted vaginal delivery), maternal infection (fever of $>38.5^{\circ}\text{C}$ during labor), hypoxic-ischemic encephalopathy (HIE) (low Apgar scores, acidosis, resuscitation, mechanical ventilation), and intracranial bleeding were considered as perinatal risk factors, and CNS infections, hypoglycemia, sepsis, cerebral hemorrhage, and stroke were considered as postnatal risk factors^{2,10,11}. Patients lacking in any pre/peri/postnatal risk factors were evaluated as an individual specific group. The patients identified as having more than one risk factor were categorized according to the dominant risk factor.

In Group 2, the cranial imaging findings (computed tomography [CT] or magnetic resonance imaging [MRI]) of the cases were classified into six groups: CNS malformations, periventricular leukomalacia (PVL), cortical/subcortical atrophy, basal ganglia/thalamic lesions, others (calcification, gliosis and hydrocephaly), and normal¹¹.

The problems accompanying CP were investigated in Groups 1 and 2 as mental retardation, epilepsy, visual or auditory problems, language developmental delay, hyperactivity and attention deficit disorder, gastroesophageal reflux (GER), and malnutrition.

Regarding database creation and statistical analysis, the Statistical Package for the Social Sciences (SPSS) for Windows v. 11.5 statistical program and Epi-info program were used. Since parametric conditions were not always met, chi-square test and Fisher's exact test were used in order to measure the effects of independent variables on the dependent variables. p values less than 0.05 were considered as significant.

Results

The male/female ratio was 1.4 and 1.7 in Groups 1 and 2, respectively. More specific demographic features are given in Table I.

Table I. Sociodemographic Characteristics of Cases

	Group 1 (n=208)		Group 2 (n=442)		p
	n	%	n	%	
Prematurity	37	17.7	168	38	0.000
Full-term delivery	124	59.6	272	61.5	
Postmaturity	14	6.7	1	0.2	
Unknown gestational age	33	15.9	1	0.2	
Birth type					0.000
Vaginal	171	82.2	235	53.2	
Cesarean section	20	9.6	187	42.3	
Assisted vaginal	17	8.2	16	3.6	
Breech presentation	NR	NR	2	0.5	
Birth place					0.000
Hospital	134	64.4	416	94.1	
Home with midwife	NR	NR	21	4.8	
Home without midwife	58	27.9	2	0.5	
Birth weight	n=131		n=428		0.000
≥ 2500 g	88	67.2	241	56.3	
VLBW (<1500 g)	2	1.5	59	13.8	
LBW (1500-2499 g)	41	31.3	128	30	

VLBW: Very low birth weight. NR: Not recorded

Table II. Types of Cerebral Palsy

Types of CP	Group 1 (n=202)		Group 2 (n=442)		p
	n	%	n	%	
Sp. tetraparesis	132	63.5	165	37.3	0.000
Sp. diparesis	16	7.7	149	33.7	
Sp. hemiparesis	30	14.4	76	17.2	
Ataxic type	6	2.9	36	8.1	
Dyskinetic type	18	8.6	16	3.6	

Sp.: Spastic.

In Group 1, 27% of deliveries were carried out at home, while the percentage of home deliveries in Group 2 was significantly lower (0.5%, $p < 0.000$).

The cesarean delivery rate significantly increased in Group 2 cases when it was compared to Group 1 (9.6% vs. 42.3%, $p < 0.000$). In Group 2, the number of premature cases significantly increased when compared to Group 1 cases (38% vs. 17.7%, $p < 0.0000$), and the same relationship was also observed in VLBW cases (13.8% vs. 1.5%, $p < 0.000$). Conversely, there was a significant decrease in the number of cases with unknown birth weight (37% vs. 3.2%, $p < 0.000$). Parental consanguinity was 16.4% and 10.4% in Groups 1 and 2, respectively.

When CP types were evaluated, it was seen that the rate of spastic diparesis had increased four-fold in Group 2. This group also presented a significant decrease in the rate of spastic tetraparesis (63.5% vs. 37.3%). Results are shown in Table II. In Group 2, there was no significant relationship between method of delivery and type of CP ($p > 0.05$).

In Group 1, 66% of parents had noticed abnormal developmental milestones in the first six months. This percentage was highest in dyskinetic patients, with 89%. In Group 2, time of diagnosis was between 3 and 36 months. The rates of diagnosis in the first year were 39.4% and 56.9% in Groups 1 and 2, respectively ($p < 0.000$). The rates of diagnosis after two years in Groups 1 and 2 were 22.6% and 8.1%, respectively ($p < 0.000$).

When the patients were evaluated etiologically, perinatal risk factors were found to be the primary cause in both groups (Group 1: 85.9% and Group 2: 81.5%). Among the perinatal risk factors, perinatal asphyxia was seen most

frequently in both groups followed by preterm birth. Premature birth occurred significantly more frequently in Group 2 ($p = 0.000$). There was no significant difference between the two groups in terms of other risk factors ($p = 0.653$) (Table III).

The Group 2 patients were evaluated in terms of gestational age and risk factors. Perinatal risk factors were found to be significantly higher in babies born prematurely than in term babies (99.4% vs. 70.7%, $p = 0.000$). Postnatal risk factors were found only in term babies (7.7%). All CP patients lacking any risk factors were term babies. No significant differences in distribution of prenatal and perinatal risk factors were detected in either LBW cases or the cases with normal birth weight ($p = 0.099$) (Table IV).

Gestational age was recorded in 175/208 cases (84.1%) in Group 1. In this group, CP types in preterm and term patients were similar (spastic tetraparesis 64.9% vs. 63%, spastic diparesis 8.1% vs. 7.3%, spastic hemiparesis 16.2% vs. 16.1%, respectively). In Group 1, no significant correlation was determined between CP types and gestational age ($p > 0.05$).

In Group 2 preterm cases, spastic tetraparesis and diparesis were observed at similar rates (41.6% vs. 43.4%). In this group, term cases had spastic tetraparesis and diparesis in 34.4% and 27.8%, respectively. In preterms, the rate of spastic diparesis was significantly higher than in term cases ($p = 0.000$). Spastic hemiparesis and ataxic type were observed more commonly in term infants (11.3% and 3.6% in preterms, 20.9% and 11% in terms, respectively), while dyskinetic type was observed only in term infants (5.9%) ($p = 0.001$). Results are shown in Table V.

In Group 1, birth weights of 131/208 patients

Table III. Distribution of Risk Factors in CP Etiology

Risk Factors	Group 1 (n=208)		Group 2 (n=442)		p	
	n	%	n	%		
Prenatal						
Intrauterine infection	7	3.3	15	3.4	0.51	
CNS malformations	6	2.9	21	4.8		
Chromosome anomalies	NR	-	3	1.8		
Maternal systemic diseases	NR	-	15	3.4		
Fetal placental insufficiency	NR	-	64	14.5		
Drug use during pregnancy	NR	-	8	1.8		
Multiple pregnancy	NR	-	27	6.1		
Perinatal						
Premature birth	37	17.7	168	38	0.000	
Perinatal asphyxia	147	71	293	66.3		
Neonatal sepsis	6	2.9	41	9.3		
Jaundice	25	12	38	8.6		
Birth complications	NR	-	105	23.8		
Convulsion	NR	-	100	22.6		
Intracranial hemorrhage	NR	-	40	9		
Preeclampsia	NR	-	12	2.7		
Postnatal						
Sepsis/CNS infection	8	3.9	23	5.2		
Trauma	NR	-	3	0.7		
Metabolic causes	NR	-	2	0.5		
Unknown	9	4	27	6.1		

NR: Not recorded. CNS: Central nervous system.

were known - 31.3% (41/131) were recorded as LBW and 1.5% (2/131) were as VLBW. In Group 1, there was no significant relationship between birth weight and type of CP ($p > 0.05$).

In Group 2, birth weights of 428/442 patients were known, and the percentages of patients with LBW and VLBW were 30% (128/428) and 13.8% (59/428), respectively. In Group 2, the rate of spastic diparesis was significantly higher in VLBW patients than in patients with LBW and normal birth weight (47.5%, 39.8% and 27%, respectively, $p = 0.005$). In Group 2, there was no significant relationship between spastic tetraparesis and birth weight. The rate of hemiparesis displayed a significant increase with increasing birth weight (8.5%, 12.5% and 20.3%, respectively, $p = 0.032$) (Table V).

In terms of associated problems in Groups 1 and 2, mental retardation ranked highest in both groups (68.3% vs. 87.3%). Epilepsy (44.2% and 45.2%) and microcephaly (31.7% and 50.2%) were also observed. Visual problems (strabismus, visual field defect, decreased visual

acuity, visual loss) in 48% of patients, hearing loss in 16%, delay in language development in 79%, and attention deficit-hyperactivity disorder in 16.5% were also observed in Group 2. Regarding these patients, no differences were observed between term and preterm patients in terms of accompanying problems ($p > 0.05$). In 6.3% of patients in Group 2, GER was detected, and the highest incidence (15.2%) was found in patients with spastic tetraparesis. Twenty-six of 28 patients with GER were treated medically and 8 were treated surgically.

Cranial imaging using CT was carried out on 132 patients in Group 1. Pathologic features were detected in 76 of these patients (57.8%). The most common pathologies were cortical atrophy with or without calcification, infarction, and porencephaly. No significant relationship was detected between CT pathology, CP type and birth weight ($p > 0.05$).

In Group 2, neuroimaging was done in the form of CT or MRI in 430 of 442 patients (97.3%). Cortical-subcortical atrophy

Table IV. Distribution of Risk Factors According to Gestational Age and Birth Weight in Group 2 Cases

Gestational Age / Birth Weight	Risk Factors						p
	Prenatal		Perinatal		Postnatal		
	n	%	n	%	n	%	
≤ 37 weeks (n=168)	1	0.6	167	99.4	NR	-	p=0.000
38-42 weeks (n=246)	32	11.7	193	70.7	21	7.7	
<1500 g (n=59)	NR	-	59	100	NR	-	p=0.099
1500-2499g (n=128)	13	10.2	113	88.3	NR	-	
≥2500 g (n=241)	19	7.9	178	73.9	19	7.9	

NR: Not recorded.

Table V. Distribution of Types of CP According to Gestational Age and Birth Weight in Group 2 Cases

Types of CP	Gestational Age				Birth Weight					
	≤37 weeks (n=168)		38-42 weeks (n=272)		<1500 g (n=59)		1500-2499 g (n=128)		≥2500 g (n=241)	
	n	%	n	%	n	%	n	%	n	%
Sp. tetraparesis	70	41.6	94	34.4	23	39.0	53	41.4	87	36.1
Sp. diparesis	73	43.4	76	27.8	28	47.5	51	39.8	65	27
Sp. hemiparesis	19	11.3	57	20.9	5	8.5	16	12.5	49	20.3
Ataxic type	6	3.6	30	11	3	5	6	4.7	26	10.8
Dyskinetic type	NR	-	16	5.9	NR	-	2	1.6	14	5.8

Sp.: Spastic. NR: Not recorded.

at 54% (232/430) and PVL at 52.3% (225/430) were the most commonly detected abnormalities. Other problems such as cystic encephalomalacia, intracranial calcification, gliosis, and hydrocephalus were observed in 36.3% (156/430) and basal ganglia lesions in 0.7% (3/430). Patients often had more than one abnormality. Neuroimaging findings were normal in only 16 patients. PVL was observed at rates of 65.5% and 42.1% in preterm and term patients, respectively. The highest incidences were found in patients also presenting with preterm spastic diparesis (83.6%).

In Group 2, 75.3% (333/442) of patients with CP had physical-therapy rehabilitation (PTR) either for a limited period or continuing, and 39.4% (174/442) benefited from training courses. For spasticity, 243 patients (55%) were treated with oral myorelaxant medication, while 46 patients (10.4%) received botulinum toxin injections. Sixty-two patients (14%) used orthotic devices. Orthopedic surgery, such as Achilles tenotomy, adductor tenotomy, and release of the hamstrings, was performed in 7.5% of cases. Two hundred and twenty patients (49.8%) were given antiepileptic treatment, but

27.2% (60/220) of these patients were found to have drug-resistant epilepsy.

Discussion

Cerebral palsy (CP) is one of the most common causes of childhood disability in our country as well as worldwide. Approximately 1.4 million babies are born annually in Turkey; considering the prevalence rate of CP of 2-2.5 per 1000 live births (reported from centers across Europe), approximately 2800-3500 children with CP will need to be integrated into the Turkish community annually. Serdaroğlu et al⁷. actually reported the incidence as higher in Turkey, with 4.4 per 1000 live births, between the ages of 2-16.

Several studies, including ours, have revealed that CP is more frequent in males^{7,11-14}. Male/female ratios in Groups 1 and 2 were 1.7/1 and 1.4/1, respectively. The rate of hospital births (64.4% vs. 94.1%) was increased in Group 2, while the rate of assisted vaginal delivery (8.2% vs. 3.6%) and unassisted home birth (27.9% vs. 0.5%) decreased. According to some authors, there is no direct association between cesarean delivery and CP, but there is

an association between cesarean delivery and prenatal CNS damage^{13,15}. In our study, the increase in cesarean delivery rate in Group 2 (42.3% vs. 9.6%) seems to support this view.

Multiple pregnancies will increase the risk of CP development since it leads to premature birth and intrauterine fetal death^{16,17}. While the multiple pregnancy rate was not defined in Group 1, it was found as 6.1% (29 patients) in Group 2.

It is generally accepted that CP risk increases as the gestational age decreases^{4,6}. In consecutive studies^{2,4,11} regarding CP, the rate of prematurity was found as 43%, 44%, and 43%, respectively. A study from the United States reported the rate as 45%¹⁸, while two Turkish studies focusing on this area presented their findings as 48.4%, and 24.8%^{7,19}. In reference to our study, in Group 2, the rate of premature infants significantly increased. This result can be explained by a reduction in perinatal mortality and improvements in preterm care.

According to several studies, spastic CP is the most frequent form of the disease^{12,14}. In the past, spastic diparesis was the most common type found in Western countries^{2,4,13}; however, spastic hemiparesis has been the most common form found recently^{11,20,21}. Interestingly, spastic diparesis (39.8%) is currently the most frequent type diagnosed in Turkey⁷. In our study, there was a significant decrease (63.5% vs. 37.3%, respectively) in the rate of spastic tetraparesis and a significant increase in the rate of spastic diparesis (7.7% vs. 33.7%) in Group 2. Rates of spastic tetraparesis and spastic diparesis were similar between 1995 and 2006. The decrease in spastic tetraparesis and the increase in diparesis over time can be explained by the improvement in prenatal, natal and neonatal intensive care and a decrease of mortality in prematures. A decrease in patients with dyskinetic type in Group 2 was also observed (3.6% vs. 8.6%). The cause of this change was considered to be prevention of bilirubin encephalopathy with early diagnosis and treatment.

Regarding the relationship between gestational age and type of CP, spastic diparesis was the most common type found in preterm infants across studies^{2,4,7}. Similarly, spastic diparesis ranked highest in preterm infants in Group 2 (43.5%), while it ranked fourth in Group 1 (8.1%). The rate of patients with spastic

hemiparesis increased in correlation with the increase in gestational age in Group 2.

Age of diagnosis was reported as 8.2 and 23.4 months in other CP studies^{22,23}. In Group 2, the average age at diagnosis was 13±6.8 months. For this group, the diagnosis rate in the first year was significantly increased (56.9% vs. 39.4%) and the rate of diagnosis after two years was significantly decreased (8.1% vs. 22.6%). The cause of this change was considered to be the implementation of follow-up for infants with CP risk beginning in the antenatal period.

Studies in developed countries have shown that when it comes to the etiology of CP, perinatal risk factors (49% - 75%) were principally responsible in preterms, while prenatal risk factors (33% - 37%) were the dominant cause in term patients. The rate of patients not presenting with any risk factors has also gradually decreased^{2,11,13,15,20,21}. In our study, we found perinatal risk factors were principally responsible in both groups (81.5% and 85.9%, respectively). HIE, which constitutes the most common cause of perinatal brain injury, has been reported at rates of 22%-80% in several studies^{11,14,22}. In Group 2, HIE was observed to a greater extent in preterm infants (72.9% in preterm vs. 62.3% in term), and the postnatal risk factors such as CNS infection, trauma and sepsis were observed at comparatively higher levels in term infants (7.7%). This presents a similar pattern to other studies^{4,7}. The fact that the higher rate of perinatal risk factors may be linked to premature birth needs to be considered, and if taken seriously, may be an indication that we have not yet reached satisfactory levels, regarding care, over a 35-year period.

Since 1990, the widespread use of surfactant and antenatal steroids has provided an increase in the rate of survival of patients with VLBW^{6,12,15,17}. Similar to this result, a significant increase was also observed in the rates of patients with VLBW (13.8% vs. 1.5%, respectively) in Group 2.

In 25%-80% of patients with CP, particularly cognitive disorders and other problems (such as epilepsy; auditory, language and visual; chronic pain; gastrointestinal and nutritional) can also be seen^{5,17}. In a multicenter study from Europe, severe cognitive impairment was recorded in

31% and severe visual impairment in 11.1%, and active epilepsy was detected in 20.7% of the patients¹². In a study from the American Academy of Neurology and Child Neurology Society⁵, it was reported that mental retardation accompanied CP in 52% of cases, epilepsy in 43%, visual impairment in 28%, hearing problems in 12%, and speech disorders in 38%. In our study, mental retardation also presented as the most common problem in both groups (68.3% in Group 1 and 87.3% in Group 2). The high rate of mental retardation in our groups may be related to the high number of patients presenting with spastic tetraparesis.

In both our groups, the rate of epilepsy was similar (44.2% and 45.2%). In Group 2, epilepsy was seen more commonly in terms (53%), and was most commonly detected in patients with spastic hemiparesis (57.9%). The highest rates of preterms with spastic tetraparesis and visual problems such as strabismus, refractive error, visual field defect, and blindness were also detected in this group (48%). Hearing problems and articulation disorders were found in 16% and 79%, respectively, and these results are consistent with the literature^{5,17,22}. GER was detected in 28 patients (6.3%) from Group 2, and this presented most frequently in patients with spastic tetraparesis. Twenty-six of 28 patients were given medical treatment and eight patients were treated surgically.

The American Academy of Neurology reported that cranial imaging techniques in infants with CP play a significant role in demonstrating the etiology and that cranial MRI was superior to CT (89% vs. 77%)⁵. In many studies, PVL was determined most frequently in patients presenting with spastic diparesis, and term-type injuries such as basal ganglia, thalamus, encephalomalacia, and subcortical atrophy were recorded in term patients^{24,25}. In Group 1, CT was obtained from 132 (62.5%) patients, and in 57.8% of them, pathological changes were found, the most common being cortical atrophy (67%). In Group 2, either cranial MRI or CT was performed in 430 (97.3%), and in 96.3% of them, abnormal findings were determined. The most frequently detected abnormalities were cortical/subcortical atrophy (54%) and PVL (52.3%). Atrophy was highest in spastic tetraparesis cases (66.1%), and PVL was most frequent in spastic diparesis

(73.8%). PVL was highest in preterms with spastic diparesis (83.6%). In 63.2% of spastic hemiparesis patients, MRI abnormalities such as intracranial calcification, gliosis, hydrocephalus, and cystic encephalomalacia were found.

The current rate of disability in Turkey stands at 12.3%. Children between the ages of 0-19 represent 8.8% of this population, and only limited numbers of these children benefit from special education institutions²⁶. In the region of our study, benefits of PTR (75.3%) and special education (39.4%) were higher than current national levels. The goal must be to provide these facilities for all patients nationally, regardless of encumbrances such as locality or level of disability.

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