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Epilepsy and Cerebral Palsy

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Abstract

Abnormalities of muscle tone, movement, and motor skills are the hallmark of cerebral palsy (CP) which results from injury to the developing brain. Clinically, the syndrome evolves over time and may only be apparent after 3–5 years of age, although suggestive signs and symptoms may be present at an earlier age. Epilepsy is common in CP and occurs in about 30% of patients. Generally, the onset is within the first 2 years of life. Epilepsy is commonly observed in children with spastic hemiplegia, followed by quadriplegia and diplegia. Significant risk factors for the development of epilepsy in patients with CP are family history, neonatal seizure, structural abnormalities, low Apgar scores, and mental retardation. Focal to bilateral tonic-clonic seizures are the most prominent seizure types, followed by focal aware or impaired awareness seizures, while infantile spasms and myoclonic jerks are seen in 25% of cases. Mental retardation is a predisposing factor for early onset of seizures and more severe epilepsy. The overall outcome of seizures in children with CP is generally poor, requiring prolonged course of antiepileptic medication, usually polytherapy with higher incidence of refractory seizures, side effects, comorbidities, and hospital admissions for drug-resistant seizures or status epilepticus.

Keywords: cerebral palsy, epilepsy, seizures, treatment, mental retardation

1. Introduction

Cerebral palsy is a term that implies a disorder of motor function. It is a neurodevelopmental abnormality affecting muscle tone, movement, and motor skills. CP is the result of a nonprogressive damage of the nervous system at its early developmental stage and can be caused by several factors encountered in prenatal, perinatal, or postnatal periods [1]. Although the disorder itself is nonprogressive, the clinical expression changes over time as the brain develops and matures.

The International Consensus in 2005 defined CP as follows [2]: “CP is a group of permanent neurological disorders resulting from nonprogressive brain injury or malformation that occurred in the developing fetal or infant brain and primarily affecting body movement, posture and muscle coordination. The motor dysfunction in CP is often associated with abnormal cognitive abilities including communication and behavior, disturbance in sensation and perception and last but not least, epilepsy and secondary musculoskeletal complications”.

There is no consensus in the literature about the prevalence of epilepsy in patients with CP. Studies indicate a very wide range of epilepsy in children with CP. However, it is argued that in certain types of CP, higher rate of epilepsy is found and that an average of 30% of patients with CP exhibit seizures. This figure is proportional to the degree of motor and cognitive disabilities [3, 4].

2. Prevalence and incidence of cerebral palsy

The estimated prevalence of CP is approximately 2 per 1000 children. The risk is even higher in preterm infants with low birth weight [5, 6].

The advances in prenatal, perinatal, and postnatal pediatric care significantly influenced the reported incidence and prevalence of CP. The most common causes of CP have varied over time and between geographical locations. While the developed world faces predominantly prematurity and extremely low-birth-weight-related morbidities, the developing countries are still faced with prenatal rubella, perinatal asphyxia, and postnatal hyperbilirubinemia.

From the 1960s to 1980s, the rate of CP and the extent of disability among preterm infants increased as survival improved for the most immature [7]. This trend reversed later, most likely because of improvements in perinatal care [8].

3. Etiology of cerebral palsy

The etiology of CP is multifactorial. Most cases are likely related to prenatal factors: among them prematurity and/or low birth weight. Other associated etiologies include congenital abnormalities, multiple pregnancy, placental pathology, intrauterine infection, metabolic encephalopathies, and genetic forms of CP.

Perinatal hypoxia and ischemia account for only a marginal number of cases of CP. Stroke in the perinatal period may cause CP and is typically manifested as spastic hemiparesis.

In an Australian study of 213 children diagnosed with CP [9], a multifactorial etiology was demonstrated. Major CP-associated pathologies, other than acute intrapartum hypoxia, were found in 98% of cases; some children had several associated pathologies such as

- Prematurity (78%).
- Intrauterine growth restriction (34%).
- Intrauterine infection (28%).
- Antepartum hemorrhage (27%).
- Severe placental pathology (21%).
- Multiple pregnancy (20%).
- Very-low-birth-weight (VLBW) infants (5–15%). In these cases, CP is frequently associated with periventricular leukomalacia, intraventricular hemorrhage, and/or bronchopulmonary dysplasia.

4. Clinical features and classification of cerebral palsy

The classification of CP is based on the type and distribution of motor abnormalities. Suggestive signs and symptoms may be present in infancy, and severe cerebral palsy can be diagnosed as early as 1 month of age. However, the specific CP syndromes are best recognized in time as the child's brain matures, e.g., spastic CP is usually diagnosed after the age of 6 months, dyskinetic CP usually after 18–20 months old, and the ataxic type even later. Following-up the children with high risk will allow early recognition and intervention.

Early diagnosis, in some cases, will enable early intervention for the child by a multidisciplinary team and in addition early psychological and possible financial support to the family.

Early signs of CP include as follows:

Neurobehavioral findings: a neonate who presents with poor feeding with or without recurrent vomiting, irritability, poor sleeping pattern, and poor visual attention should raise suspicion of CP. In addition, prolonged retention or exaggeration of these primitive reflexes is often a premature sign of motor disability. In infants with hyperactive tonic labyrinthine reflex, opisthotonus may occur, or they may roll over at an earlier age than usually expected. Similarly, children with CP may present inadequate posture in vertical suspension in that they present persistent extension of lower extremities on attempting a sitting position.

Motor tone and posture: Tone can be normal in some subjects, but it may be increased or decreased in the extremities of others.

Delay in sitting without support beyond 9 months, poor head control, persistent or asymmetric hand fisting beyond 4 months, and abnormal oromotor patterns (tongue thrusting or grimacing) are often the early motor signs. Sometimes increased neck extensor and axial tone may make head control appears better than it is.

The abovementioned features may also coincide with intellectual impairment, hemianopia, and other visual problems. Also, behavioral problems are frequently found among children with hemiplegic CP including anxiety and specific phobias.

After age 18–24 months, signs and symptoms generally align to a specific subtype of CP:

Spastic CP includes spastic diplegia, spastic hemiplegia, and spastic quadriplegia, with accompanying features pointing to an upper motor neuron syndrome like spastic hypertonia, hyperreflexia, extensor plantar responses, and Dyskinetic CP is characterized by involuntary, stereotyped, uncontrolled, recurring movements of athetosis, chorea, and dystonia.

CP associated with ataxic movements (loss of orderly muscular coordination, unstable gait) and speech is referred to as ataxic CP and is usually associated with a widespread disorder of motor function. Ataxic CP is rare, and children who present with these findings must be evaluated for other potential causes of ataxia.

Mixed CP is a spastic type with ataxic and/or dyskinetic features of variable predominance.

Hypotonic CP is not included in the contemporary classifications. Majority of patients with “hypotonic CP” in early infancy later develop spastic, dyskinetic, or ataxic CP. **Table 1** shows the proportion of the different types of CP.

Spastic subtypes	Percentages (%)
Spastic diplegia	13–25
Spastic hemiplegia	21–40
Spastic quadriplegia	20–43
Dyskinetic subtypes	12–14
Ataxic CP	4–13

Table 1.
Proportion of the different types of cerebral palsy.

5. Associated comorbidities

Besides motor disabilities, there are significant comorbid disorders of cerebral function that may appear or become severe as the child grows including intellectual disability, seizures, behavioral and emotional disorders, speech and language disorders, as well as visual and hearing impairments. Social difficulties and autism spectrum disorders are also commonly associated comorbidities [10]. In addition, many accompanying conditions such as growth failure, pulmonary disease, orthopedic problems (e.g., joint subluxations and dislocations and hip dysplasia), osteopenia, urinary disorders, sleep disturbance, and hypersalivation have been identified. Pain is common in children with CP and can significantly impact the quality of life. Children with more severe motor disabilities are also more likely to have comorbidities.

These associated comorbidities occur in CP at variable rates. Pain is noted in 75% of CP subjects, intellectual disability in half of them, whereas inability to walk or hip displacement is equally seen in a third. Twenty-five percent of children with CP cannot talk, and a similar proportion carries a diagnosis of epilepsy. Behavioral disorders and urinary incontinence are equally seen in roughly 25% of subjects and sleep disorders in 20%; tube feeding is needed in little less than 10%. Blindness is noted in 10% of cases, with deafness being less common at a rate of 5%.

6. Neuroimaging in cerebral palsy

Head CT scan commonly identifies abnormalities, particularly in spastic CP. Cerebral atrophy is a frequent finding in quadriplegia, whereas infarction, porencephalic cyst, and cerebral atrophy occur equally (26.7%) in hemiplegic CP, and periventricular leukomalacia is significantly more common with diplegia. A brain abnormality seen on CT scan has been reported in 77% of the cases of hemiplegia, followed by quadriplegia (75%) and diplegia (55%) [11], while other studies showed CT abnormalities in 77.2% of patients, with bilateral atrophy in 42.1% and focal findings in 17.6% of the cases [12].

MRI scan is an important and safe diagnostic tool to use in children with CP after 18 months in order to assess location, nature, and structure of brain lesion and correlate findings with clinical picture.

The patterns of MRI in children with cerebral palsy are as follows:

- White matter damage, observed more often in spastic diplegia and quadriplegia.

- Gray matter damage: central gray matter damage of acute perinatal hypoxia-ischemia in term infants is associated with death and CP.
- Enlarged ventricles, bilateral or unilateral, abnormalities of the atria and ventricular or occipital horns, and posterior fossa, atrophy, and cerebrospinal fluid abnormalities [13].

In a European cerebral palsy study [14], MRI was performed in 351 of the 431 children with clinically assessed CP. The MRI scans showed that white matter damage of immaturity, including periventricular leukomalacia, was the most common finding (42.5%, majority born before 34 weeks), followed by basal ganglia lesions (12.8%), cortical/subcortical lesions (9.4%), malformations (9.1%), focal infarcts (7.4%), and miscellaneous lesions (7.1%). Normal MRI findings were present in 11.7%.

MRI scan does provide useful information on the timing and extent of the lesion. Predisposing risk factors include maternal and child genetic factors in thrombophilia leading to stroke, nutritional factors, and infections during

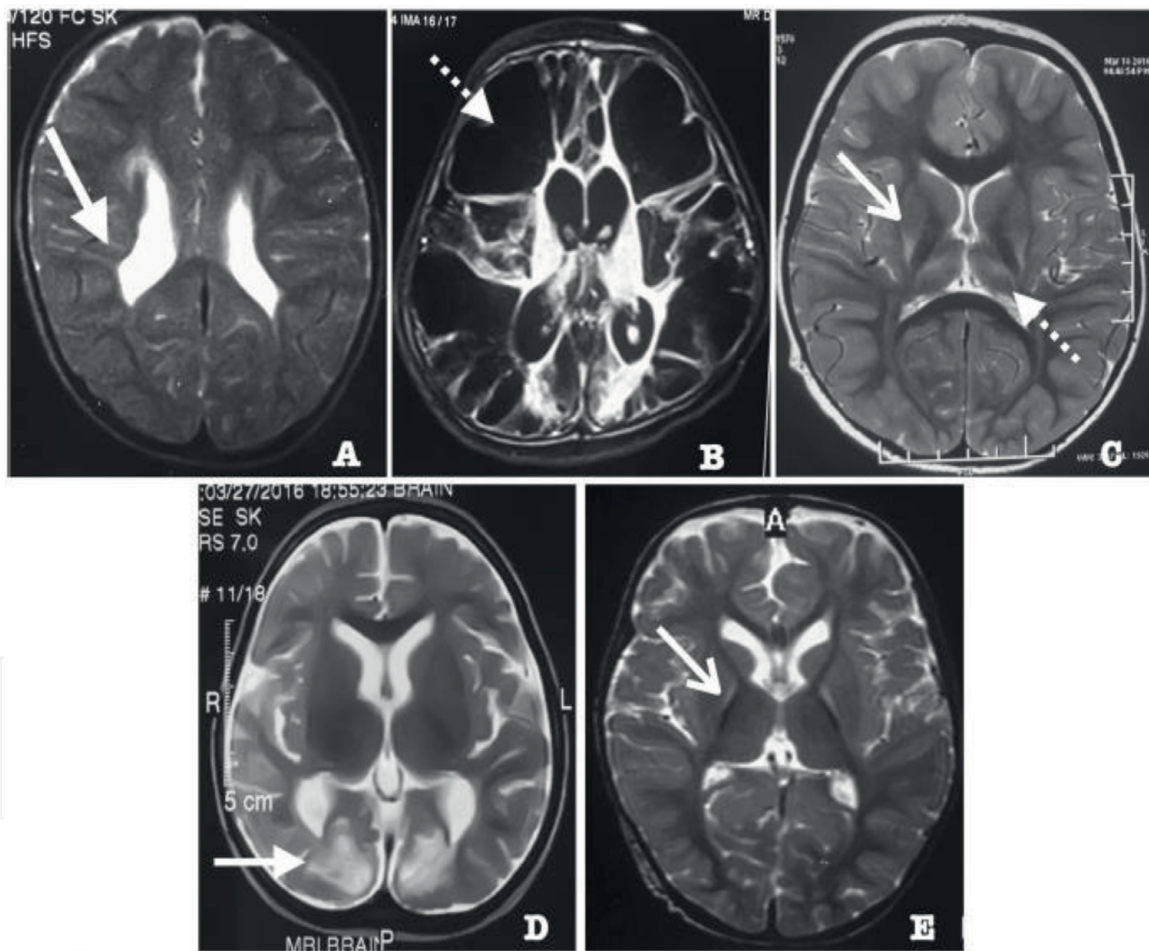


Figure 1. Salient MRI changes in cerebral palsy. Panel A shows a T2-weighted image with periventricular hyperintensities and undulating ventricular margins (solid arrow). This is typically seen in prematurity associated insult and commonly manifests as spastic diplegia. Panel B shows multicystic encephalomalacia (dotted line with arrow). This pattern of watershed lesions is seen commonly in term infants with ischemia/asphyxia and manifests clinically with spastic quadriplegia. Panel C illustrates T2 hyperintensities in posterior putamen (open arrow) and thalami bilaterally (dotted line with closed arrow). This is typically seen in infants with term hypoxic ischemic encephalopathy (HIE) and manifests as dyskinetic cerebral palsy. Panel D highlights T2 hyperintensities in occipital lobe (solid arrow); characteristic of neonatal hypoglycemic insult. Panel E shows T2 hyperintensity involving bilateral globus pallidi (open arrow), a feature of kernicterus sequelae.

pregnancy and before the onset of premature labor lead to placental damage developing throughout the pregnancy. These factors predispose the infant to an increased risk of hypoxic ischemic episodes, leading to white matter damage.

It is not unreasonable, therefore, to assume that with increased awareness of possible preventive measures, CP could be reduced substantially, reducing as a consequence the burden on families and saving tremendous sums of money for health services. **Figure 1** shows the MRI findings in CP.

7. Evaluation of patient with cerebral palsy

The diagnostic evaluation must include standardized assessment of neurologic and motor development and magnetic resonance imaging (MRI).

Screening for thrombophilia is recommended in children with MRI evidence of cerebral infarction.

Other testing depends on clinical and anamnestic concerns and may include:

- Metabolic and genetic testing, which should be pursued in the presence of atypical symptoms or MRI findings (e.g., a brain malformation or injury) or if no etiology is identified by clinical history and neuroimaging
- Electroencephalogram (EEG) if seizure activity is suspected
- Infectious work-up (TORCH titers) if pre- or perinatal history is suggestive

All children with CP need to be screened for commonly associated conditions, such as intellectual disability, ophthalmologic abnormalities, hearing impairment, speech and language disorders, and growth failure.

8. Diagnosis of cerebral palsy

A combination of clinical findings supports the diagnosis of CP; a single clinical finding is generally not sufficient to establish the diagnosis.

Key features in the diagnosis of CP include:

1. Abnormal motor development and posture.
2. Brain injury is permanent and nonprogressive.
3. Motor impairment is attributed to an insult that occurred in the developing fetal or infant brain.
4. Motor impairment results in limitations in functional abilities and activities.
5. Motor impairment is often accompanied by secondary musculoskeletal problems, epilepsy, and/or disturbances of sensation, perception, cognition, communication, and behavior.

9. Prognosis of cerebral palsy

Survival to adulthood is currently a standard for most children. An analysis of children with CP born in different geographical areas of the United Kingdom

between 1980 and 1996 revealed a 20-year survival in 87–94% of cases [15]. The multivariate analysis revealed that survival was related to severity of impairment, birth weight, and socioeconomic status, with the number of severe impairments having the greatest effect.

Those children who do not achieve head balance by 20 months retain primitive reflexes, have no postural reactions by 24 months, or do not crawl by approximately 5 years of age have generally poor prognosis for walking. Generally, all children with hemiplegic CP and many with athetosis or ataxia will walk. Those who walk independently do so around the age of 3; those who walk only with support may take up to 9 years. Those who do not walk by 9 years of age are unlikely to ever walk, even with support [16].

Functional outcome in CP also depends on other non-motor factors. These include intelligence, physical function, ability to communicate, and personality attributes.

10. Seizures in cerebral palsy patients

Besides the motor dysfunction, epilepsy is another important problem in children with CP. It is sometimes more disabling than the motor disorder itself.

10.1 Incidence of seizures and epilepsy in CP

Epilepsy is highly correlated with CP.

The incidence of epilepsy in CP varies from 33 to 41% [11, 12]. The incidence and type of epilepsy vary according to the type of CP.

The large variation in percentages reported in the literature can be explained in part by the variable length of follow-up periods and the different average age of studied subjects.

Reported rates of seizures and epilepsy in CP vary significantly depending on the underlying pathology and etiology. Epilepsy occurs in 50–94% of children with CP due to diffuse cortical malformations and injuries [17, 18] and in 50% of children with CP secondary to suspected perinatal arterial ischemic stroke [19, 20]. Epilepsy occurs at a much lower frequency (26–43%) in CP and white matter injury (WMI) than in other etiologies [21–24]. The lower frequency of epilepsy and WMI is related to the lack of involvement of cortical gray matter. A recent publication [25] indicated that 25% of children with CP and WMI had seizures beyond the neonatal period with electroclinical features of the age-limited, epileptic syndromes of childhood, with favorable outcome in the majority. Very interesting findings that need to be confirmed, guiding toward better diagnostic, treatment, prognostic, and genetic issues at this early age group.

Seizure onset often occurs in the first 2 years of life. Sixty-one percent of patients with CP had their seizure onset that early. Some reports indicate 36.7% [12] to 69.7% [23] of patients with seizure onset in the first year of life. The onset of epilepsy probably reflects the time of occurrence of brain damage and its severity.

The age of seizure onset also depends on the type of CP. Over 60% of the children with quadriplegia and diplegia have seizures in their first year of life, while 60% of the children with hemiplegia had their first seizure at a later age. Children with myoclonic seizures and infantile spasms had seizure onset very early in life [11].

10.2 Risk factors for seizures in patients with CP

Family history, structural abnormalities (primarily brain atrophy and gray matter involvement), neonatal seizure, low Apgar scores, and mental retardation are significant risk factors for the development of epilepsy in patients with CP.

CP patients with spastic quadriplegia or acquired hemiplegia are more prone to seizures, whereas seizures are less common in mild symmetric spastic diplegia and CP that is mainly athetoid.

The mode of delivery, the relative birth weight, head circumferences, and the presence of consanguinity are not known to be risk factors for epilepsy in these patients.

Risk factors for the development of epilepsy are shown in **Table 2**.

In a study of 452 patients with CP and 160 patients with both CP and epilepsy [11], the incidence of epilepsy among patients with hemiparetic CP was 65.9%, compared to 42.6% in patients with quadriparetic CP and 15.8% in patients with paraparetic CP. The different levels and degrees of brain damage may account for the various percentages.

Other studies revealed that epilepsy was found in 54% of quadriparetic, 34–60% of hemiparetic, 27% of diparetic, and 23–26% of dystonic CP patients [26, 27].

The age at onset of seizures might differ depending on the type of CP. Carlsson et al. reported the seizure onset of age as 6 months in quadriparetic CP, 12 months in diparetic CP, and 2.5 years in hemiparetic CP [21].

10.2.1 Neonatal seizures

Neonatal seizures represent a strong predictor for the development of epilepsy. A strong association of neonatal seizures with epilepsy was reported in the Collaborative Perinatal Project (NCP) of the NIH summarizing 54,000 singleton pregnancies between 1959 and 1966 [28]. Subsequently, additional retrospective studies provided clear evidence that in children with CP neonatal seizures were strongly predictive for future development of epilepsy [11, 29].

Neonatal seizure history in patients with CP is a risk factor for epilepsy development. In addition, the outcome for seizure control was negatively affected by this history, and patients with neonatal seizure history are 3.3 times more likely to have poor epilepsy prognosis than those who had no neonatal seizure history [30].

	CP With Epilepsy n = 62	CP Without Epilepsy n = 38	
Girl/boy	29/33	19/19	Ns
Neonatal seizures	30	3	p < 0.004
Positive family history	18	1	P < 0.02
CT scan abnormalities	48/57*	15/27**	Ns

Ns, not significant; *48 of 57 patients with CP and epilepsy showed computed tomographic scan abnormalities; **15 of 27 patients with CP and without epilepsy showed computed tomographic scan abnormalities.

Table 2.
Type of CP as a risk factor for seizures.

Hence, neonatal seizure history in CP is a significant risk factor for both epilepsy development and poor epilepsy prognosis.

10.2.2 Family history of epilepsy

Family history of epilepsy is associated with a 5.5 times higher risk of epilepsy in patients with CP [31].

10.2.3 Mental retardation

Mental retardation is more frequently observed in CP patients with seizures than in those without seizures, and severe mental retardation is more likely in those with multiple seizure types.

In patients with CP and mental retardation, the diagnosis of epilepsy presents unique challenges. Generally, patients are unable to describe the epileptic events themselves, parents may not recognize subtle seizure manifestations, and persons trained in epilepsy witness the events only rarely.

Mental retardation is frequently observed in patients with both CP and epilepsy compared to patients with CP only. In addition, the risk of epilepsy development is higher in patients with CP who have mental retardation [32, 33].

Patients with CP and epilepsy have lower intelligence levels compared with CP alone; the patients with paroxysmal abnormalities in the EEG had lower intelligence levels and learning disabilities [34].

Mental retardation is most common in quadriplegic CP, followed by hemiplegic CP. On the contrary, almost half of diplegic CP and 60% of children with dystonic CP have normal to borderline intelligence, which again correlates well with the type and location of brain damage. Mental retardation is associated with earlier age of onset, increased frequency, and treatment-resistant seizures [11]. This might represent an underlying severity of brain injury that is responsible for the severity of both cognitive deficit and epilepsy.

10.2.4 Apgar score and risk of seizures in CP patients

The risk of epilepsy is inversely proportional to the Apgar scores of term babies, both at 5 and 10 minutes. This is significant even with relatively minor reductions in these scores [35].

Low Apgar scores were also recognized as risk factors for epilepsy in the general population in some other studies [36, 37].

No relationship has been found between the risk of epilepsy development and gestational age [31]. In a study where 173 patients were categorized according to their birth weight as appropriate for gestational age (76.9%), small for gestational age (12.1%), and large for gestational age (11%), they found no correlation between birth weight and risk of epilepsy development [38].

However, other studies reveal that low birth weight and prematurity increase the risk of epilepsy development in patients with CP [12, 37, 39]. These studies assessed Apgar scores and determined that premature babies have lower Apgar scores; they suggested that the increased risk of epilepsy development among premature babies was actually related to low Apgar scores.

10.3 Types of seizures

All types of epileptic seizures can be seen in patients with CP. Focal impaired awareness (complex partial) and focal to generalized tonic-clonic are the most

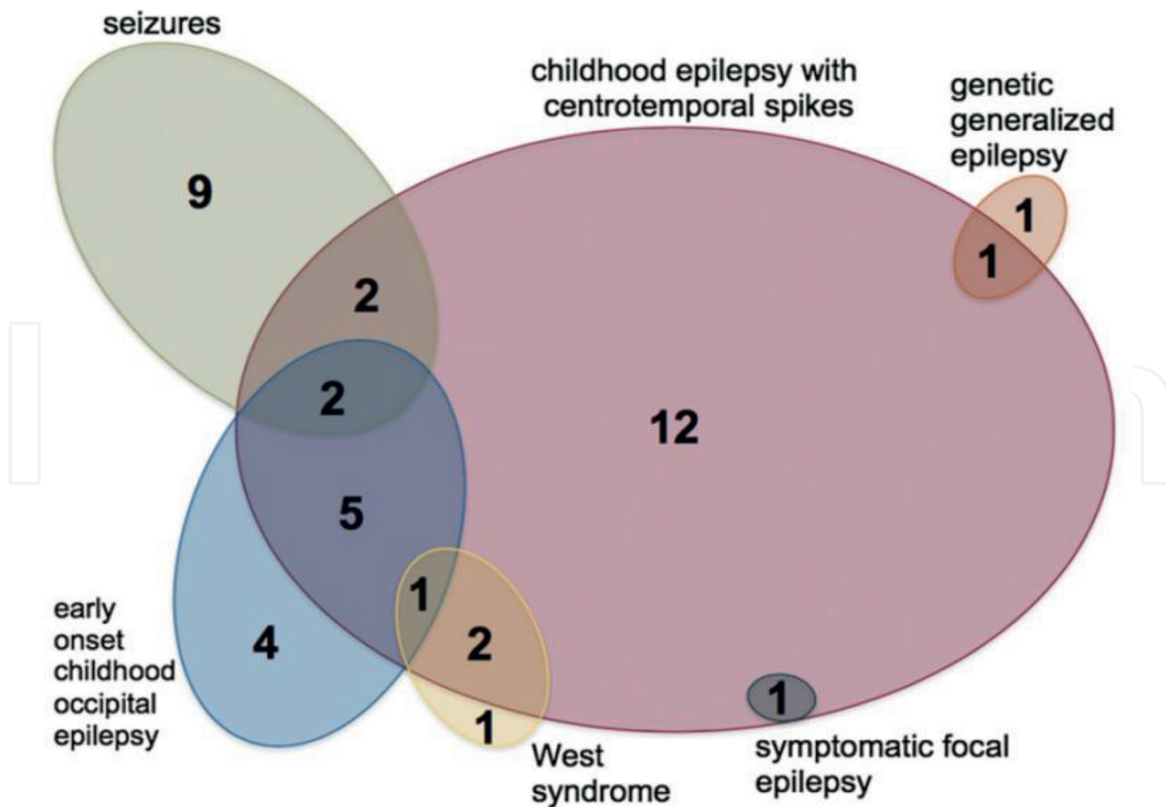


Figure 2.
Epileptic syndromes in 41 children with cerebral palsy.

Seizure Type	SPQ (n = 53)	SPD (n = 20)	SPH (n = 22)	DYS (n = 5)	HYPO (n = 3)	Mixed (n = 2)	Overall (n = 105)
GTC	19 (35.1%)	9 (45%)	7 (31.8%)	1 (20%)	3 (100%)	1 (50%)	40 (38.1%)
SP	3 (5.7%)	3 (15%)	1 (4.5%)	1 (20%)	0	1 (50%)	9 (8.6%)
CP	6 (11.3%)	1 (5%)	6 (27.3%)	0	0	0	13 (12.4%)
P-SG	7 (13.2%)	3 (15%)	3 (13.6%)	0	0	0	13 (12.4%)
MJ	9 (17%)	3 (15%)	1 (4.5%)	2 (40%)	0	0	15 (14.3%)
IS	14 (26.4%)	5 (25%)	3 (13.6%)	1 (20%)	0	0	23 (22%)
Others	0	1 (5%)	0	0	0	0	1 (1%)

CP = complex partial; DYS = dyskinetic; GTC = generalized tonic clonic; HYPO = hypotonic; IS = infantile spasms; MJ = myoclonic jerks; P-SG = partial with secondary generalization; SP = simple partial; SPD = spastic diplegia; SPH = spastic hemiplegia; SPQ = spastic quadriplegia.

Table 3.
Types of seizures in subtypes of CP [11].

frequent seizure types. Some syndromes, such as infantile spasms, West, and Lennox-Gastaut syndromes, are particularly frequent.

Generalized epilepsy is the predominant form of epilepsy in CP. Generalized seizures have been reported in 36.8%, followed by focal (partial) seizures in 33%, West syndrome in 15.6%, and myoclonic jerks in 10.6%. Absence seizures are usually of the atypical type reported in 3.3–6.7% [3].

In another study of patients with both CP and epilepsy, the following seizure types were observed: 44.6% experience focal to generalized tonic-clonic, 41.1%

focal impaired awareness (complex partial), 7.1% focal aware (simple partial), 5.4% myoclonic, and 1.8% experience atonic seizures [30]. This finding is in line with the literature review [31]. **Figure 2** and **Table 3** show epileptic syndromes and types of seizures in subtypes of CP in children with cerebral palsy.

10.4 Electroencephalogram (EEG)

EEG is essential in the work-up of children with CP and suspected seizures. It can lend support to the diagnosis of epilepsy and assist in seizure/epilepsy classification to better guide the choice of antiseizure drugs. However, there is no clinical value of performing EEG testing in children with no suggestion of seizure activity by history, and EEG testing is not useful in establishing the cause of CP.

The rate of EEG abnormalities observed in patients with CP and epilepsy is in the range of 66–92.6% [4, 11, 31].

All of the subgroups of spastic CP had a greater than 70% incidence of abnormal EEGs. Whereas in quadriplegic and diplegic CP, the EEG shows predominant bilateral epileptic activity; about half of children with hemiplegia had focal findings. In a study of children with CP and epilepsy, only 7.9% of children had normal interictal EEGs [Table 4] [4].

There was a correlation between brain CT scan and EEG findings; children with bilateral brain abnormalities on their CT scan imaging often had bilateral and generalized epileptiform abnormalities on their EEGs. However, one-fourth of these children had a focal epileptiform abnormality with rapid bilateral synchrony. On the other hand, 35.3% of children with unilateral structural brain abnormalities on their CT scans had focal epileptiform abnormalities in their EEG recordings; the EEG findings were concordant with the CT scan findings in all patients [11].

10.5 Neuroimaging in cerebral palsy with epilepsy

Children with CP and epilepsy appear to have abnormal brain imaging more often. It is not surprising that a trend toward the occurrence of epilepsy was found in children with gray matter insult (primarily cerebral infarcts), rather than in children with white matter lesions. In addition, cerebral atrophy was also reported more frequently in CP complicated by epilepsy [31], reaching statistical significance in the study of Gururaj et al. [40]. A possible explanation for the association of

EEG	SPQ (n = 53)	SPD (n = 20)	SPH (n = 22)	DYS (n = 5)	HYPQ (n = 3)	Mixed (n = 2)	Total (n = 105)
Generalized activity	21	10	9	2	2	0	44
Focal activity	5	2	4	2	0	0	13
Focal onset—							
bilateral synchrony	10	3	3	0	0	1	7
Total	36 (67.9%)	15 (75%)	16 (72.7%)	4 (80%)	2 (66.6%)	1 (50%)	74 (70.5%)

DYS = dyskinetic; HYPQ = hypotonic; SPD = spastic diplegia; SPH = spastic hemiplegia; SPQ = spastic quadriplegia.

Table 4.
 EEG abnormality and type of CP.

Imaging findings	CP Only	CP & Epilepsy	Total
Normal imaging	25 (28.7%)	10 (16.4%)	35 (23.6%)
Abnormal Imaging (all findings)	62 (71.3%)	51 (83.6%)	113 (76.4%)
Non-specific atrophy	4 (4.6 %)	11 (18.0%)	16 (10.8%)
Grey matter insult (including infarctions)	14 (16.1%)	17 (27.9%)	31 (21.0%)
White matter insult (including PVL)	16 (18.4%)	4 (11.5%)	23 (15.5%)
Cerebral malformations Dysgenesis	10 (11.5%)	7 (11.5%)	17 (11.5%)
Hydrocephalus	5 (5.7%)	5 (8.2%)	8 (5.4%)
Brain Hemorrhage (including IVH)	13 (14.9%)	7 (11.5%)	20 (13.5%)
Total	87 (100%)	61 (100%)	148 (100%)

Abbreviations: PVL – Periventricular Leukomalacia, and IVH – Intraventricular Hemorrhage.
 $p < 0.003$.

Table 5.
Imaging findings in patients with cerebral palsy only and with cerebral palsy and epilepsy.

atrophy and epilepsy is the fact that in many cases atrophy presents the end result of prenatal or perinatal global ischemia with extensive neuronal damage.

Intraventricular hemorrhage was identified as a significant risk factor for the development of neonatal seizures [41]. In patients with neonatal seizures, cerebral dysgenesis and intraventricular hemorrhage proved to be predictors for poor outcome [29].

Brain imaging in children with CP and epilepsy shows frequently abnormal findings. In children with CP and epilepsy, cerebral atrophy is more often reported [31, 40]. Atrophy is the consequence of prenatal and perinatal ischemia; this will lead to an extensive neuronal damage which may be the cause of the seizures. A significant risk factor for the development of neonatal seizures was found with intraventricular hemorrhage [41]. Cerebral dysgenesis and intraventricular hemorrhage were found to be predictors of poor outcome in patients with neonatal seizures [29].

The effect of imaging abnormalities in CP remains controversial. In one study, an MRI abnormality was noted in 86.7% of patients, and the abnormal finding variable in the MRI did not significantly affect the epilepsy development and seizure outcome.

In other studies the range of abnormal findings in MRI was reported as 84–88% [42]. Cerebral infarct is found by neuroimaging to be an abnormality that significantly affects seizure outcome in epileptic patients with CP [4]. **Table 5** shows the imaging findings in patients with CP and epilepsy and CP without epilepsy.

10.6 Seizure control

More than 50% of seizures in patients with CP are fairly controlled. Seizures in patients with hemiplegic CP achieve better control (75%) than those with quadriplegic and diplegic CP (50%); one study reported seizure control in children with CP in nearly two-thirds [4]. Seizure control was achieved with monotherapy in the majority of cases. Polytherapy was required in half, one-third, and one-fourth of cases with diplegic, quadriplegic, and hemiplegic CP, respectively, although this difference did not reach statistical significance. In another study by Hadjipanayis et al., children with spastic hemiplegia (35%) and tetraplegia (28%) were more likely to require polytherapy compared to patients with spastic diplegia (11%) [3]; however, the differences were not statistically significant [3]. Not surprising, polytherapy was required more often in children with infantile spasms and myoclonic seizures. All other seizure characteristics also were more severe in the group requiring polytherapy. In addition, a trend was noted for the following: seizures began earlier, and CT and EEG abnormalities were more often present in children requiring polytherapy.

10.7 Cerebral palsy: recommendation and future directions

The rate of CP has remained static for decades, at between 2 and 2.5 cases for every 1000 live births, due to abnormalities of the developing fetal or infantile brain resulting from a variety of causes. In a recent publication, however, Hollung et al. reported that the prevalence of CP declined for children born in Norway from 2.62 per 1000 in 1999 to 1.89 in 2010, and in addition a substantial improvement in the severity of clinical characteristics with a decrease in the proportion of children with severe motor impairments, epilepsy, intellectual disability, and difficult to understand or no speech was observed. They attributed this improvement to the better obstetric and neonatal care the first decade of the twenty-first century [43]. In general, however, methods that have been implemented, such as continuous electronic monitoring of the fetus in labor, have not had the anticipated benefits. Many neuroprotective strategies have failed. In premature infants, an increase in survival without a decrease in prevalence added more healthy citizens but also more disabled children to the population. As a consequence in recent years, efforts have focused on prevention, cure, early diagnosis, and early intervention in an attempt to reduce further CP prevalence.

Approximately one-half of all new cases of cerebral palsy arise from the group of neonates born prematurely (< 30 weeks gestation) that are at risk for long-term neurodevelopmental problems, with almost one-half having motor, cognitive, and/or language impairments, a rate much higher than their term peers [44]. For many children, however, the cause of cerebral palsy is unclear. There are many known risk factors that affect the fetal and neonatal developing brain leading to cerebral palsy, and some of them can be prevented. Risk factors for congenital CP include infection during pregnancy (toxoplasmosis, rubella, cytomegalovirus, and herpes can infect the womb and placenta, leading to brain damage in the fetus), abuses of alcohol or drugs during pregnancy, smoking, exposure to toxic chemicals, multiple gestations, and infertility treatments that have an increased risk in preterm delivery and multiple gestations and certain medical conditions such as diabetes, high blood pressure, abnormal thyroid function, sexually transmitted infections, and eating disorders (anorexia nervosa, bulimia nervosa, binge eating disorder). Placental infarctions are most likely to be identified in the births of infants who will in the

future develop cerebral palsy, especially those with spastic quadriplegia, an early reliable biomarker.

Before pregnancy we have to make sure that the woman is protected against certain diseases such as rubella with vaccination and certain preventable infections or cytomegalovirus (CMV). CMV in particular, is transmitted through close person-to-person contact with infected secretions such as in urine and saliva. The infection is transmitted from the mother to the fetus during pregnancy and can sometimes cause stillbirth, premature birth, and neurological conditions such as cerebral palsy. Children with cerebral palsy infected with CMV are more likely to have spastic quadriplegia, severe functional mobility limitations and a range of associated impairments including epilepsy, deafness, vision impairment, and moderate-to-severe intellectual disabilities, than children born with cerebral palsy but without CMV. There is evidence that public health approaches based on hygiene can dramatically reduce the rate of primary maternal cytomegalovirus infections during pregnancy. Formulated consensus recommendations on the diagnosis, prevention, and treatment of maternal and congenital CMV infection are found in the publication of Rawlinson et al. [45].

Our primary aim, therefore, is to provide a healthy pregnancy by advising and treating appropriately treatable conditions and introduce current preventable strategies and interventions that hold promise for reducing the prevalence of cerebral palsy. Such interventions include strategies to decrease the risk of premature birth (e.g., 17α -progesterone), limit the number of multiple gestations related to assisted reproductive technology, treat mothers who are expected to deliver prior to 30 weeks gestation with magnesium sulfate for fetal neuroprotection that can prevent cerebral palsy, give antenatal steroids for mothers expected to deliver prematurely, caffeine for extremely low-birth-weight neonates, and induce hypothermia for a subgroup of neonates diagnosed with intrapartum hypoxic-ischemic encephalopathy [46]. Hypothermia, either selectively applied to the head or total body, appears to decrease the risk of cerebral palsy [47]. Interventions which either prolong gestation or decrease the risk of preterm delivery will also decrease the risk of cerebral palsy.

Although ~50% of very preterm children has neurodevelopmental impairments, an early prediction of infants who will experience problems later in life still remains an early diagnostic challenge. White matter abnormalities (WMA) at term have been associated with CP in very preterm children and can be used as a biomarker for early multidisciplinary approach. Very preterm children with any WMA at term require follow-up throughout childhood [48]. Abnormal general movements in very preterm infants born <30 weeks gestation, particularly at 3 months post term, are predictive of worse neurodevelopment at ages 2 and 4 years and need multidisciplinary approach. The accuracy for predicting moderate to severe cognitive impairment was good at 83% and 77% for 2 and 4 years, respectively [49].

Recent research on neuroplasticity supports intensive, repetitive, task-specific intervention for CP that should commence early while the brain is most plastic. Early postnatal recognition is important for a prompt referral to diagnostic-specific early intervention setting to optimize infant's motor and cognitive plasticity, prevent secondary complications, and enhance caregiver's well-being [50].

Beside traditional conventional therapies, physical therapy, occupational therapy, and speech-language therapy, a number of other approaches have been used such as the use of Botox, selective dorsal rhizotomy, functional vision assessment and intervention programs, developmental optometry, biofeedback, hippotherapy, hyperbaric oxygen therapy, deep brain stimulation for dyskinetic forms of cerebral palsy, stem cell applications, and even yoga. It is very difficult to decide which method is "gold standard" type of therapy for CP because it is impossible to conduct

double-blind, randomized control trials. However, identifying predictive biomarkers and developing preventive strategies phenotypically orientated to different subsyndromes, we can prevent or intervene early taking into consideration the advantage of brain plasticity.

11. Conclusions

In general children with CP have epileptic seizures in about one-third that occur as a rule within the first 2 years of life. The most common seizure type is focal generalized seizures followed by focal, infantile spasms, and myoclonic seizures that are seen in one-fourth of cases. Seizures are most often seen in spastic hemiplegia and spastic quadriplegia. Children with CP and mental retardation have an early onset of seizures and more severe epilepsy. The response to antiseizure treatment in children with CP is generally difficult, and one-third to half of the cases is receiving polytherapy and/or alternative therapies.

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References

- [1] Mutch L, Alberman E, Hagberg B, et al. Cerebral palsy epidemiology: Where are we now and where are we going? *Developmental Medicine & Child Neurology*. 1992;**34**:547-551
- [2] The definition and classification of cerebral palsy. *Developmental Medicine and Child Neurology*. 2007;**49**:1-44
- [3] Hadjipanayis A, Hadjichristodoulou C, Youroukos S. Epilepsy in patients with cerebral palsy. *Developmental Medicine and Child Neurology*. 1997;**39**:659-663
- [4] Zafeiriou D, Eleftherios E, Kontopoulos E, Tsikoulas I. Characteristics and prognosis of epilepsy in children with cerebral palsy. *Journal of Child Neurology*. 1999;**14**:289-294
- [5] Oskoui M, Coutinho F, Dykeman J, et al. An update on the prevalence of cerebral palsy: A systematic review and meta-analysis. *Developmental Medicine and Child Neurology*. 2013;**55**:509
- [6] Hirvonen M, Ojala R, Korhonen P, et al. Cerebral palsy among children born moderately and late preterm. *Pediatrics*. 2014;**134**:e1584
- [7] Pharoah PO, Platt MJ, Cooke T. The changing epidemiology of cerebral palsy. *Archives of Disease in Childhood. Fetal and Neonatal Edition*. 1996;**75**:F169
- [8] Platt MJ, Cans C, Johnson A, et al. Trends in cerebral palsy among infants of very low birthweight (<1500 g) or born prematurely (<32 weeks) in 16 European centres: A database study. *Lancet*. 2007;**369**:43
- [9] Strijbis EM, Oudman I, van Essen P, MacLennan AH. Cerebral palsy and the application of the international criteria for acute intrapartum hypoxia. *Obstetrics & Gynecology*. 2006, 107:1357
- [10] Venter A, Schirm N, Joubert G, Fock J. Profile of children diagnosed with cerebral palsy at universitas hospital, Bloemfontein, 1991–2001. *South African Family Practice*. 2006;**48**:15. Available from: <http://www.tandfonline.com/doi/abs/10.1080/20786204.2006.1087335>
- [11] Novak I, Hines M, Goldsmith S, Barclay R. Clinical prognostic messages from a systematic review on cerebral palsy. *Pediatrics*. 2012;**130**(5):e1285-e1312
- [12] Singhi P, Jagirdar S, Khandelwal N, Malhi P. Epilepsy in children with cerebral palsy. *Journal of Child Neurology*. 2003;**18**:174e9
- [13] Pedersen H, Taudorf K, Melchior JC. Computed tomography in spastic cerebral palsy. *Neuroradiology*. 1982;**23**:275-278
- [14] Aksu F. Nature and prognosis of seizures in patients with cerebral palsy. *Developmental Medicine and Child Neurology*. 1990;**32**:661-668
- [15] Bjorgaas H, Elgen I, Boe T, Hysing M. Mental health in children with cerebral palsy: Does screening capture the complexity? Hindawi publishing corporation. *The Scientific World Journal*. 2013;**4**:1-8
- [16] Mirmiran M, Barnes P, Keller K, Constantinou J, Fleisher B, Hintz S, et al. Magnetic resonance imaging findings in a population-based cohort of children with cerebral palsy. *The Journal of Pediatrics*. 2004;**114**(4):992-998
- [17] Bax M, Tydeman C, Flodmark O. Clinical and MRI correlates of cerebral palsy. *The European cerebral palsy study*. *JAMA*. 2006;**296**(13):1602-1608

- [18] Rosenbaum P, Paneth N, Leviton A, et al. A report: The definition and classification of cerebral palsy April 2006. *Developmental Medicine and Child Neurology. Supplement.* 2007; **109**:8
- [19] Hemming K, Hutton JL, Colver A, Platt MJ. Regional variation in survival of people with cerebral palsy in the United Kingdom. *Pediatrics.* 2005; **116**: 1383-1390
- [20] da Paz Junior AC, Burnett SM, Braga LW. Walking prognosis in cerebral palsy: A 22-year retrospective analysis. *Developmental Medicine and Child Neurology.* 1994; **36**:130-134
- [21] Reid SM, Dagia CD, Ditchfield MR, Reddihough DS. Grey matter injury patterns in cerebral palsy: Associations between structural involvement on MRI and clinical outcomes. *Developmental Medicine and Child Neurology.* 2015; **57**(12):1159-1167
- [22] Carlsson M, Hagberg G, Olsson I. Clinical and aetiological aspects of epilepsy in children with cerebral palsy. *Developmental Medicine and Child Neurology.* 2003; **45**(6):371-376
- [23] Wanigasinghe J, Reid SM, Mackay MT, Reddihough DS, Harvey AS, Freeman JL. Epilepsy in hemiplegic cerebral palsy due to perinatal arterial ischaemic stroke. *Developmental Medicine and Child Neurology.* 2010; **52**(11):1021-1027
- [24] Fukuda K, Kirino T, Fujiwara Y, Nagai S, Endo S. Clinical aspects of epilepsy in children with periventricular leukomalacia [in Japanese]. *No to Hattatsu.* 2010; **42**(4):291-295
- [25] Cooper MS, Mackay MT, Fahey M, Reddihough D, Reid SM, Williams K, et al. Seizures in children with cerebral palsy and white matter injury. *Pediatrics.* 2017; **139**(3):e20162975
- [26] Aicardi J. Epilepsy in brain injured children. *Developmental Medicine and Child Neurology.* 1990; **32**:191e202
- [27] Jacobs IB. Epilepsy. In: Thompson GH, Rubin IL, Bilenker RM, editors. *Comprehensive Management of Cerebral Palsy.* New York: Grune and Stratton; 1983. p. 131e7
- [28] Nelson KB, Ellenberg JH. Antecedents of seizure disorders in early childhood. *American Journal of Diseases of Children.* 1986; **140**:1053-1061
- [29] Ronen GM, Buckley D, Penney S, Streiner DL. Long-term prognosis in children with neonatal seizures: A populationbased study. *Neurology.* 2007; **69**:1816-1822
- [30] Mert GG, Incecik F, Altunbasak S, Herguner O, Mert MK, Kiris N, et al. Factors affecting epilepsy development and epilepsy prognosis in cerebral palsy. *Pediatric Neurology.* 2011; **45**(2):89-94
- [31] Kulak W, Sobaniec W. Risk factors and prognosis of epilepsy in children with cerebral palsy in North-Eastern Poland. *Brain Development.* 2003; **27**: 499e506
- [32] Goulden KJ, Shinnar S, Koller H. Epilepsy in children with mental retardation: A chart study. *Epilepsia.* 1991; **32**:690e7
- [33] Steffenberg U, Hagberg G, Kyllerman M. Characteristics of seizures in a population- based series of mentally retarded children with active epilepsy. *Epilepsia.* 1996; **37**:850e6
- [34] Wallace SJ. Epilepsy in cerebral palsy. *Developmental Medicine and Child Neurology.* 2001; **43**:713e7
- [35] Persson M, Razaz N, Tedroff K, Joseph KS, Cnattingius S. Five and 10 minute Apgar scores and risks of cerebral palsy and epilepsy: Population

based cohort study in Sweden. *BMJ*. 2018;**360**:k207

[36] Sun Y, Vestergaard M, Pedersen CB, Christensen J, Olsen J. Apgar scores and long-term risk of epilepsy. *Epidemiology*. 2006;**17**:296-301

[37] Ehrenstein V, Sørensen HT, Pedersen L, Larsen H, Holsteen V, Rothman KJ. Apgar score and hospitalization for epilepsy in childhood: A registry-based cohort study. *BMC Public Health*. 2006;**6**:23

[38] Zelnik N, Konopnicki M, Bennett-Back O, Castel-Dutch T, Tirosh E. Risk factors for epilepsy in children with cerebral palsy. *European Journal of Paediatric Neurology*. 2009;**30**:1e6

[39] Odding E, Roebroek ME, Stam HJ. The epidemiology of cerebral palsy: Incidence, impairments and risk factors. *Disability and Rehabilitation*. 2006;**28**: 183e91

[40] Gururaj AK, Sztrihá L, Bener A, Dawadou A, Eapen V. Epilepsy in children with cerebral palsy. *Seizure*. 2003;**12**:110e4

[41] Kohelet D, Shochat R, Lusky A, Reichman B. Israel neonatal network. Risk factors for seizures in very low birthweight infants with periventricular leukomalacia. *Journal of Child Neurology*. 2006;**21**:965-970

[42] Robinson MN, Peake JL, Ditchfield MR, Reid MS, Lanigan A, Reddihough DS. Magnetic resonance imaging findings in a population based cohort of children with cerebral epilepsy. *Developmental Medicine and Child Neurology*. 2008;**51**:39e45

[43] Hollung SJ, Vik T, Lydersen S, Bakken IJ, Andersen GL. Decreasing prevalence and severity of cerebral palsy in Norway among children born 1999 to 2010 concomitant with improvements in perinatal health.

European Journal of Paediatric Neurology. 2018;**22**:814-821

[44] Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. *Lancet*. 2008;**371**(9608):261-269

[45] Rawlinson WD, Boppana SB, Fowler KB, et al. Congenital cytomegalovirus infection in pregnancy and the neonate: Consensus recommendations for prevention, diagnosis, and therapy. *The Lancet Infectious Diseases*. 2017;**17**(6): e177-e188

[46] O'Shea TM. Diagnosis, treatment, and prevention of cerebral palsy in near-term/term infants. *Clinical Obstetrics and Gynecology*. 2008;**51**(4):816-828. DOI: 10.1097/GRF.0b013e3181870ba7

[47] Shankaran S, Laptook AR, Ehrenkranz RA, Tyson JE, McDonald SA, Donovan EF, et al. Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. *New England Journal of Medicine*. 2005;**353**(15): 1574-1584

[48] Spittle AJ, Cheong J, Doyle LW, Roberts G, Lee JK, Lim J, et al. Neonatal white matter abnormality predicts childhood motor impairment in very preterm children. *Developmental Medicine and Child Neurology*. 2011; **53**(11):1000-1006. DOI: 10.1111/j.1469-8749.2011.04095.x

[49] Spittle AJ, Spencer-Smith MM, Cheong JL, Eeles AL, et al. General movements in very preterm children and neurodevelopment at 2 and 4 years. *Pediatrics*. 2013;**132**(12):e452-e458

[50] Novak I, Morgan C, Adde L, Blackman J, Boyd RN, et al. Early, Accurate Diagnosis and Early Intervention in Cerebral Palsy: Advances in Diagnosis and Treatment. *JAMA Pediatrics*. 2017;**171**(9): 897-907