Evaluation of risk factors for cerebral palsy

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Abstract

Background: Cerebral palsy (CP) has been identified as one of the most important and common causes of childhood disabilities worldwide and is often accompanied by multiple comorbidities. CP is defined as a group of disorders of the development of movement and posture, causing activity limitation that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The objective of our study was to describe main clinical pattern and motor impairments of our patients, and to evaluate the presence of risk factors and if there is a relation to the type of cerebral palsy.

Methods: Children with cerebral palsy were retrospectively enrolled over 2 years from the neurology outpatient clinics. Cerebral palsy risk factors and motor impairments were determined through caregiver interviews, review of medical records, and direct physical examination.

Results: One thousand children with cerebral palsy were enrolled. Subjects were 64.4% male, with a median age of 2.5 years. The risk factors for cerebral palsy in our study were antenatal (21%), natal and post-natal (30.5%), post-neonatal (17.1%), and unidentified (31.4%). Antenatal as CNS malformation (26.6%), maternal DM (17.6%), prolonged rupture of membrane (11.9%), maternal hemorrhage (10.4%), and pre-eclampsia (4.7%). Natal and post-natal as hypoxic ischemic encephalopathy (28.5%), infection (16.3%), hyperbilirubinemia (12.7%), cerebrovascular accidents (8.8%), meconium aspiration (6.2%), and intracranial hemorrhage. Post-neonatal as CNS infection (34.5%), cerebrovascular accidents (28.6%), sepsis (23.9%), and intracranial hemorrhage (8.7%).

Conclusions: Cerebral palsy has different etiologies and risk factors. Further studies are necessary to determine optimal preventative strategies in these patients.

Keywords: Cerebral palsy, Central nervous system, Risk factors, Motor impairments

Introduction

Cerebral palsy (CP) is the most common motor disorder among children as its worldwide prevalence is ranging from 1.5 to more than 4 per 1000 live births or children of a defined age range [1]. However, CP appeared to be more prevalent in low- or middle-income countries than in high-income countries [2]. CP prevalence was about 3.6 and 2.9 per 1000 children in Uganda and Egypt, respectively, but the prevalence was 1.8 to 2.3 cases per 1000 children in the USA, Europe, and Australia [3, 4].

Cerebral palsy (CP) describes a group of disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. It begins in early childhood and persists through the lifespan [5].

It was first reported as a movement disorder in the historical documents of the Sumerians, and Hippocrates [6].

Cerebral palsy (CP) is the major cause of motor impairment in young children [7, 8] The clinical picture changes over time [9], and a recent review showed that referral for diagnosis typically happens between 10 and 21 months of age [10].

Even patients with the same motor impairment are not the same, and that is why the development of functional scales has been an important step in management of CP patients. The Gross Motor Function Classification System (GMFCS), a standardized observational instrument for
children with cerebral palsy, is developed to measure change in gross motor function over time. Both the GMFCS feature a 5-level ordinal scale which reflects, in a decreasing order, the level of independence and functionality of children with CP [11].

Cerebral palsy is associated with a variety of comorbidities such as visual impairment, epilepsy, cognitive impairment, disturbances of sensation, communication, perception, and behavior disorder [12]. In many children with cerebral palsy, associated comorbidities are the major drivers of outcome and quality of life [13].

Cerebral palsy is divided, according to the Reference and Training Manual of the Surveillance of Cerebral Palsy in Europe (SCPE), based on motor deficit into three groups: spastic type, dyskinetic, or ataxic, with dyskinesia which is subdivided into choreoathetosis and dystonia. Although, it is important to mention that many children have mixed presentations [14].

It is increasingly apparent that CP can result from the interaction of multiple risk factors. Its etiology is multifactorial, heterogenous, and is characterized by an injury to the immature brain. And in many cases, no identifiable cause can be found [15].

Many risk factors are identified during antenatal, natal, and post-natal periods, including multiple births, intrauterine infection, preterm, perinatal stroke, birth asphyxia, perinatal infection, placental pathology, and congenital malformations [16–19].

At the present time, it is unrealistic to determine and clear-categorize the cause; however, we should do every possible effort to evaluate causal pathways or causes.

If there is a clear evidence indicating that a major component of the cause, or the cause was operative in a certain time window, so insult timing could be determined, as a previously well infant with post-natal meningitis. However, it is important to record adverse events during pregnancy and the perinatal period of cerebral palsy, and it is not sufficient to depend on the presence of such events as causes for the cerebral palsy genesis in the affected patient [20].

The objective of this study was to describe main clinical pattern and motor impairments of our patients with cerebral palsy, and to evaluate the presence of risk factors and if there is a relation to the type of cerebral palsy.

Methods

Patients

This study was carried out in the neurology outpatient clinics. One thousand patients were recruited over 2 years consecutively based on the definition of cerebral palsy, inclusion, and exclusion criteria.

The cerebral palsy definition in our study was adopted from the International Workshop on Definition and Classification of Cerebral Palsy which defines (CP) as a group of disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behavior, and/or by a seizure disorder [21].

Inclusion criteria

Patients met all of the following inclusion criteria: (1) all patients fulfill the above definition, and (2) children ages 6 months to 16 years.

Exclusion criteria

Presence of one or more of the following: (1) hypotonic patients less than 2 years; (2) progressive condition is identified to cause the movement, development, and posture disorder; and (3) children with identified chromosomal abnormalities or syndromatic features.

Methods

All data were collected by a single assessor, directly from the families, in a special data sheet that was kept in the patient’s medical records. These data included:

1. Descriptive data regarding patients’ age, residence, and contact details.
2. Data exploring risk factors.
   These aimed at exploring different risk factors that are known to have a role in the development of CP. Risk factors were divided according to the timing of brain insult into antenatal, natal, post-natal, and post-neonatal. Antenatal referred to the period of pregnancy until the onset of labor resulting in delivery, natal, and post-natal period referred to the period from the onset of labor until the 28th day of life, and post-neonatal to the period from day 29 to 2 years of age [22].

Antenatal data

Gestational age: birth at term at more than 36 weeks, moderately preterm at 32–36 weeks, very preterm at 28–31 weeks, and extremely preterm birth was defined as birth occurring before 28 completed gestational weeks [23].

Polarity

Singleton pregnancy refers to the carriage of one fetus in the uterus, twin pregnancy refers to two fetuses, and triplets indicate three fetuses [24].

Congenital brain malformation was defined as an antenatal developmental abnormality of the brain with excluding post-natal developmental anomaly (acquired hydrocephaly and microcephaly) [25].
Antepartum hemorrhage (APH) is defined as bleeding occurring from 24 + 0 weeks of pregnancy and prior to the birth of the baby, into or from the genital tract [26].

Congenital infection is defined as a vertically transmitted infection from the mother to an embryo, fetus, or baby during pregnancy or childbirth and persist after birth and or immunologic evidence of intra-uterine infection [27].

Preeclampsia is defined as hypertension and proteinuria, with or without pathologic edema occurring after 20 weeks of gestation [28].

Prolonged rupture of membrane (PROM) is defined as membrane rupture more than 24 h [29].

Other maternal disorders included fever of > 38.5 °C before delivery indicating infection, or pre-existing chronic disorder: thyroid problems, pharmacological treatment (antibiotics and anti-epileptics), and diabetes mellitus [30].

Natal and post-natal data

Hypoxic-ischemic encephalopathy (HIE) was considered in children born at > 36 weeks of gestation in the presence of ≥ 2 of the following symptoms or signs: (a) Apgar score < 5 at 1 or 5 min; (b) resuscitation and subsequent mechanical ventilation; and (c) convulsions before day 3 [31].

Hyperbilirubinemia was defined as a risk factor if the level of bilirubin at the neonatal period was above phototherapy level or (15–20 mg/dL) and/or there were neurological symptoms at the same time at which bilirubin was high (tone, cry, posturing, eye movements).

Intracranial hemorrhage (ICH) was considered only if there was an imaging finding (CT or MRI) to support such a diagnosis.

An infectious etiology required documented summary (from the NICU) with the source of infection, results of cultures, and antibiotics used.

Emergency cesarean section (CS) was defined if there was failure to progress in labor that necessitated surgical interference at the discretion of the attending obstetrician.

The criteria for the diagnosis of meconium aspiration syndrome (MAS) include history of meconium-stained amniotic fluid before delivery or meconium covering the baby at delivery and the presence of meconium below the vocal cords at the time of birth in infants > 37 weeks of gestation.

Post-neonatal risk factors

Central nervous system infection (meningitis and encephalitis), sepsis, and accidental injury were considered if reported in the medical record or a patient discharge summary. Cerebrovascular accidents required a supporting radiology imaging.

Unidentified

This was reported when all the above risk factors were negative in the patient.

The patients were classified into four major classifications: spastic, hypotonic, dyskinetic, and ataxic subtypes, with dyskinesia further differentiated into dystonia and choreoathetosis. The spastic subtype is further subdivided into spastic hemiplegia (when there is affection of one upper and one lower limb), spastic quadriplegia (when the four limbs are involved), and spastic diplegia (when the legs are usually more affected than the arms).

Statistical analysis

Statistical analysis was done by using SPSS (statistical package for Social Science) program version 19 (2009). Normality of data was tested by one sample Kolmogorov-Smirnov test.

Our data were parametric; they were presented as mean and SD. The following statistical tests were used: chi-square and Fisher’s exact tests. Significance was considered at $p < 0.05$.

Results

The present study was carried out on 1000 cases of cerebral palsy with their mean age was 37.5 months, 64.4% were males, 71.2% from Dakahlia, 10.3% from Gharbia, 6.2% from Damietta, 4.8% from Sharkia, 4.6% from Kafr El Sheikh, and 1.9% from Port Said Governorates. According to gestational age of the studied CP cases, 69.5% were full term, 25.8% were preterm, and 4.7% were 4.7%.

Singleton infants represents 94.6% twins 4.9% and triplets 0.5%. Among identified risk factors, 30.7% of the risk factors were identified at natal and post-natal periods, 21% at antenatal period, 17.1% at post-neonatal period. According to type of motor impairment, 71.6% were spastic and 45.2% were quadriplegic (Table 1).

There is statistically significant association between antenatal risk factors and gestational age among studied CP cases with the following distribution of risk factors among preterm and post-term infants: 8.9% of cases with CNS malformation, 62.9% of cases with maternal hemorrhage, 13.6% of cases with congenital infection, 23.1% of cases with history of preeclampsia, 56.8% of cases with maternal diabetes, 71.5% of cases with maternal thyroid, 30.0% of cases with teratogenic risk factors, and 88% of cases with prolonged rupture of membrane.

Regarding natal and post-natal risk factors, 2.3% of HIE, 76.9% of neonatal sepsis, 76.7% of cases with intracranial hemorrhage, and 100.0% of cases with meconium aspiration were not full term with statistically significant relation between them. All post-neonatal risk factors were significantly associated with higher incidence of preterm and post-term; 66.7% of accidental injury, 65.9% sepsis, and 56.3% intracranial hemorrhage (Table 2).
Regarding types of cerebral palsy among studied infants, there is no statistically significant association between motor type and their gestational age while topographic appearance of spastic and mixed groups illustrates statistically significant association with gestational age with the following distribution among cases who were not full term; 54.8% were diplegic, 30% diplegic, and 14.5% hemiplegic (Table 3).

Topographic appearance of cerebral palsy was significantly associated with antenatal and unidentified risk factors. Antenatal risk factors were detected among 210 of the studied cases with 39.8% of them were hypotonic; 34.9% of cases with post-neonatal history were dyskinetic and among the unidentified causes, and 51.4% were spastic quadriplegic CP (Table 4).
| Antenatal risk factors | Total number | Not full term N = 305 (%) | Full term N = 695 (%) | p value* |
|------------------------|--------------|---------------------------|-----------------------|----------|
| n = 210               | n = 79       | n = 131                   | 0.01*                 |
| CNS malformation       | 56           | 5(8.9)                    | 51(91.1)              | 0.001*   |
| Maternal hemorrhage    | 27           | 17(62.9)                  | 10(37.1)              | 0.003*   |
| Maternal fever at delivery | 13        | 0(0.0)                    | 13(100)               | 0.003*   |
| Congenital infection   | 22           | 3(13.6)                   | 19(86.4)              | 0.014*   |
| Preeclampsia           | 13           | 3(23.1)                   | 10(76.9)              | 0.26     |
| Maternal diabetes      | 37           | 21(56.8)                  | 16(43.2)              | 0.008*   |
| Maternal thyroid       | 7            | 5(71.5)                   | 2(28.5)               | 0.06     |
| Teratogenic            | 10           | 3(30.0)                   | 7(70.0)               | 0.61     |
| Prolonged rupture of membrane | 25      | 22(88)                    | 3(12)                 | < 0.001* |

| Natal/post-natal risk factor | Total number | Not full term N = 305 (%) | Full term N = 695 (%) | p value* |
|------------------------------|--------------|---------------------------|-----------------------|----------|
| n = 307                      | n = 147      | n = 160                   | < 0.0001*             |
| HIE                          | 87           | 2(2.3)                    | 85(97.7)              | < 0.001* |
| Neonatal sepsis             | 50           | 40(76.9)                  | 12(23.1)              | < 0.001* |
| Hyperbilirubinemia          | 39           | 17(43.6)                  | 22(56.4)              | 0.566    |
| Emergency CS                | 58           | 34(58.6)                  | 24(41.4)              | 0.07     |
| Intracranial hemorrhage     | 43           | 33(76.7)                  | 10(23.3)              | 0.0004*  |
| Meconium aspiration         | 19           | 19(100.0)                 | 0(0.0)                | < 0.001* |
| Cord prolapse               | 9            | 2(22.2)                   | 7(77.8)               | 0.117    |

| Post-neonatal risk factor | Total number | Not full term N = 305 (%) | Full term N = 695 (%) | p value* |
|---------------------------|--------------|---------------------------|-----------------------|----------|
| n = 171                   | n = 47       | n = 124                   | 0.35                  |
| CNS infection             | 59           | 5(8.5)                    | 54(91.5)              | < 0.001* |
| Accidental injury         | 6            | 4(66.7)                   | 2(33.3)               | 0.049*   |
| Cerebrovascular accidents | 49           | 2(4.1)                    | 47(95.9)              | < 0.001* |
| Sepsis                    | 41           | 27(65.9)                  | 14(34.1)              | < 0.001* |
| Intracranial hemorrhage   | 16           | 9(56.3)                   | 7(43.7)               | 0.006*   |
| Unidentified              | n = 312      | 32(10.3)                  | 280(89.7)             | < 0.001* |

Tests used: chi-square test, Fisher’s exact test
*Statistically significant

| Table 3 Association between gestational age and types of cerebral palsy among studied cases |
|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|
| Motor type of CP                           | Total number | Not full term N = 305 (%) | Full term N = 695 (%) | p value* |
| Spastic                                    | 716           | 214(70.2)                  | 502(72.2)              | 0.505    |
| Dyskinetic                                 | 83            | 28(9.1)                    | 55(7.9)                | 0.504    |
| Mixed                                      | 103           | 34(9.2)                    | 69 (9.9)               | 0.559    |
| Hypotonic                                  | 98            | 29(9.5)                    | 69 (9.9)               | 0.837    |

| Topographic appearance of spastic and mixed groups | Total number | Not full term N = 305 (%) | Full term N = 695 (%) | p value* |
|---------------------------------------------------|--------------|---------------------------|-----------------------|----------|
| Hemiplegic                                        | 187          | 36(14.5)                  | 151(26.4)             | 0.001*   |
| Diplegic                                          | 262          | 136(54.8)                 | 126 (22.1)            | <0.001*  |
| Quadriplegic                                      | 370          | 76(30.7)                  | 294(51.5)             | <0.001*  |

*Statistically significant
A statistically significant association was found between moderate preterm and clinical types of cerebral palsy; 73.1% of hypo type were moderate preterm, 54.2% of dyskinetic type were very preterm and 32.2% of hemiplegic were extreme preterm (Table 5).

**Discussion**

Cerebral palsy (CP) is the most common motor disability of childhood. This hospital based study aimed at understanding the patterns and causes of CP in our locality. The results showed that 71.2% of the study population were from El Dakahlia; however, these data can neither represent the true prevalence of CP in the district nor that there is a higher rate of CP in El Dakahlia.

It is found in our study that the male:female ratio was 1.8:1. This finding is similar to the findings in other studies, as Swedish ratio of 1.55:1 was reported [32]. The male embryo is suggested at a greater risk of damage or death [33]. Stillbirth, premature birth, congenital deformities, perinatal brain damage, and neonatal adverse outcomes are more common in male [34].

In our study, identifying risk factors was tricky due to multiple reasons. First, there are at least four health systems in Egypt (Ministry of Health, university hospitals, private sectors, and insurance hospitals), and there is no national guidelines applied for prenatal care, delivery, and management of neonatal problems. Secondly, there is lack of documentation of pregnancy, delivery, and neonatal periods. Only few neonatal care units give discharge summary for the parents about the period the baby stayed in the hospital. Thirdly, most of CP cases present to the clinics after their first birthday. Since we depended on the history given by parents, discharge, or follow-up documents (if present) in identifying risk factors, there is always the possibility that parents are uncertain about events that happened in pregnancy and delivery.

We have classified risk factors according to the time of injury into (antenatal, natal/post-natal, and post-neonatal). We have evaluated gestational age and multiple births as separate groups apart from these risk factors, and then we have identified the most common risk factors in each gestational age group.

In approximately two thirds of all children with CP in this study, a major risk factor was identified. Natal and post-natal risk factors were more predominant representing 30.5%, antenatal risk factors represent 21%, and post-neonatal represent 17.1%. No reliable risk factor could be established in 31.1% of cases. This could be explained by deficient history, reliable documents, or other risk factors that were beyond the scope of the study. However, this proportion of patients is similar to that reported in other series [35, 36].

It is found in our study that most patients (69.5%, n = 695) were born at term and this is similar to many studies. This can be explained by the fact that there is more full-term than preterm infants born at a given time [37].

Multiple birth is a risk factor for CP 5.4% (54 patients) with 31 patients were preterm (64.8 %) in our study. This is also found in an European study that multiple births are at < 4 times greater risk than singletons for CP data [38]. This may be related to intra-uterine death of a triplet or a co-twin or the higher rate of prematurity [38, 39]. And also, it is related to the fertility medications and increasing age of mother [40].

Table 4: Association between identified risk factors according to the time of injury and topographic appearance of cerebral palsy among studied cases

| Risk factors       | Total N = 1000 | Spastic diplegic N = 262(%) | Spastic quadriplegic N = 370(%) | Spastic hemiplegic N = 187(%) | Dyskinetic N = 83(%) | Hypotonic N = 98(%) |
|--------------------|----------------|-----------------------------|---------------------------------|-------------------------------|---------------------|---------------------|
| Antenatal          | 210            | 73(27.9)                    | 31(8.3)                         | 59(31.5)                      | 8(7.7)              | 39(39.8)            |
| Natal/post-natal   | 307            | 93(35.5)                    | 106(28.6)                       | 58(31.1)                      | 21(25.3)            | 29(29.4)            |
| Post-neonatal      | 171            | 31(17.8)                    | 43(25.1)                        | 37(36.2)                      | 39(43.9)            | 0.001*              |
| Unidentified       | 312            | 65(24.8)                    | 190(51.4)                       | 27(14.5)                      | 25(30.1)            | 5(1.6)              |

*p value* statistically significant

Table 5: Association between preterm degree and clinical types of cerebral palsy of the studied cases

| Preterm Type       | Total N = 1000 | Hemiplegic N = 28(%) | Diplegic N = 133(%) | Quadruplegic N = 47(%) | Dyskinetic N = 24(%) | Hypo N = 26(%) |
|--------------------|---------------|----------------------|---------------------|-----------------------|---------------------|----------------|
| Moderate PT (32–36 weeks) | 105           | 11(39.2)             | 53(39.8)            | 17(36.2)              | 5(20.8)             | 19(73.1)       |
| Very PT (28–31 weeks)  | 94            | 8(28.6)              | 50(37.6)            | 19(40.4)              | 13(54.2)            | 4(15.4)        |
| Extreme PT (< 28 weeks) | 59            | 9(32.2)              | 30(22.5)            | 11(23.4)              | 6(25)               | 3(11.5)        |

*p value* statistically significant
Antenatal risk factors evaluated in this study included some of the most frequent risk factors as PROM of long duration [41], maternal medications (antibiotics and anti-epileptics) during pregnancy [42], antepartum fever [43], vaginal bleeding, pre-eclampsia, and CNS malformation [44].

In this study, CNS malformation represented 6.5% of all cases with CP. These included primary microcephaly, hydrocephaly, congenital reduction defects (holoprosencephaly), corpus callosum anomalies, and cerebellar hypoplasia. This is close to the results obtained by another study in which cerebral malformation represent 8.6% of all CP patients [45]. Cerebral malformations can be of genetic or acquired origin. The exact pathogenesis and etiology of congenital brain malformations frequently remain unknown. However, genetic and environmental factors (toxins and infectious agents) seem to play a role [46].

Maternal infection suggested by (fever around delivery, prolonged rupture of membrane and documented congenital infection) represented around 6%. This is a very low percentage in comparison to other studies which reported up to 16–23% of their cases to be due to maternal infection. Both of these studies were retrospective studies evaluated maternal files for antenatal risk factors of CP [43, 47].

Maternal conditions (DM, thyroid diseases, medications during pregnancy) represented 5.4% of all CP patients in this study. This is similar to other studies [22, 48].

When evaluating antenatal risk factors in relation to gestational age, we found that CNS malformation, congenital infection, and pre-eclampsia were more common in FT. Maternal hemorrhage, prolonged rupture of membrane, maternal DM, and thyroid diseases were more significant in preterm patients. These results are similar to other studies [26, 45].

Many studies found association between CP and emergency CS [47]. In this study, 5.8% of all CP patients were delivered by emergency CS. This was prominent with PT (51.7%) than FT (47.3%). However, we depended solely on the history from the mother and there was no explanation on why this emergency CS was done or whether the fetus had any distress before delivery or not.

Meconium aspiration occurred in 19 cases (1.9%) in this study, and all were post-term (> 42 weeks). Cord prolapsed was identified in 9 patients: 7 of them were FT and 2 were post-term. Both conditions indicate fetal distress; however, this was not supported in our study by data about fetal heart rate or cord blood PH to indicate perinatal asphyxia. The effect of amniotic fluid stained with meconium is still unclear [49, 50].

It is considered that the presence and severity of hypoxic ischemic encephalopathy during neonatal period is the strongest predictor of CP. HIE affects full term (> 37 weeks) [51]. In this study, 8.7% (n = 87) of the babies experienced neonatal encephalopathy and 97.7% of them were FT. One study estimated HIE to be a risk factor of CP in 8–15% of term patients [52].

Sepsis has been proven to increase the risk of developing CP especially in preterm [53]. In this study, sepsis in the first month of life was identified in 50 patients and 38 were preterm.

Intracranial hemorrhage in the first month of life was identified radiologically in 43 patients and 26 were preterm (60%). This result is similar to other results in which 66% of preterm patients with ICH developed CP [54].

Kernicterus continues to be a significant problem in developing countries despite progress in the management of hyperbilirubinemia. In a clinic-based review in Nigeria, it was found that hyperbilirubinemia was the most common cause of cerebral palsy [55]. In this study, jaundice was a major risk factor in 39 patients and 56% were FT.

When evaluating natal/post-natal risk factors in relation to gestational age, we found that certain factors are more common in certain age group. HIE, cord prolapse, and high jaundice were more predominant in FT. MAS was detected only in post-term. Emergency CS, sepsis, and intracranial hemorrhage were more common in PT.

Few studies evaluated post-neonatal risk factors; one is the SCPE follow-up study that evaluated post-neonatal risk factors in cerebral palsy patients from age 28 days to 25 months. Infection, vascular episodes, and head injury were the most common risk factors [56]. In this study, CNS infection was identified in 59 patients, CVA in 49 patients, sepsis in 41 patients, ICH in 16 patients, and accidental injury in 6 patients. It is worth mentioning that 10 patients out of the 16 with ICH were diagnosed as late hemorrhagic disease of newborn, which is a preventable risk factor. Out of the group of the 49 patients with CVA, 16 were diagnosed with congenital cyanotic heart diseases. CNS infection and CVA were significantly more common in FT. Sepsis, ICH, and accidental injury were common in PT.

We evaluated the different risk factors collectively in relation to gestational age and that showed that patients with natal/post-natal risk factors represented 30.5% of all cases with CP and natal/post-natal risk factors were more predominant in all gestational age groups (23% of the FT, 42.9% of the PT, and 74.4% of the post-term). This is against recent studies that found antenatal risk factors to be more predominant in different gestational ages [22]. Multiple causes may attribute to these results: (1) poor antenatal data regarding maternal pregnancy and events immediately before delivery. (2) The type of the study being a hospital based rather than population-based studies. (3) The fact that MUCH is a children hospital with a tertiary neonatal unit, referral from the unit constitutes a considerable number of patients.
Patients in this study were classified from the motor perspective into spastic (71.4%), dyskinetic (8.3%), hypotonic (9.8%), and mixed spastic with dyskinesia (10.3%). This is similar to many studies, which found that dyskinetic CP 10–20% and spastic type 80% [26, 57]. It is important to mention that some studies do not include hypotonic children as a subtype; this is due to the assumption that most hypotonic patients are believed to develop to other motor types later in their life or becomes diagnosed with other conditions that are not included under the term CP.

The spastic type of CP was the predominant motor type in the full term and preterm (72.2% and 70%). The non-spastic types are more in full term. This is similar to results by Eveline Himpens and his colleagues [58].

Regarding the topographic distribution of spastic and mixed patients, 45% of spastic patients had 4 limbs involvement, 31.9% had involvement of their lower limbs, and 22.8% have involvement of one side of the body (hemiplegic). Monoplegic patients (when one limb is only affected) were classified as hemiplegic. This is due to the fact that their motor, etiological, and functional behavior is the same.

Epidemiological studies have shown that topographic classification varies according to gestation. Spastic diplegia is more with preterm as in our study [59]. It is found that spastic hemiplegia is more common in full-term babies, and this finding is similar to other studies [60]. The proportion of spastic quadriplegia was more predominant in the term patients (79.4%) than preterm (12.7%). This is different than other studies that showed that quadriplegic CP was equal in all age groups [26, 61].

Identifying the etiologic profile of cerebral palsy types is important as each group had specific risk factors and identifying it helps understanding the potential mechanisms of pathogenesis [62]. We found that each group exhibits a different etiologic spectrum. The spastic diplegic group had the natal/post-natal risk factors as the most common (34.7%). The dyskinetic group had more post-neonatal causes than other group. Unidentified risk factors were more predominant in the quadriplegic patients (51.3%).

Conclusion
Cerebral palsy has different etiologies and risk factors.

Recommendations
We recommend to address preventable causes of CP which can help to establish better practice as reduction of multiple births after infertility treatment, vitamin K administration to prevent late hemorrhagic disease, and early efficient management of jaundice.

The group of patients with cerebral malformation represent a special group that needs further studies to evaluate risk factors related to it, and whether environmental factors, genetic predisposition (2ry to relative marriage) plays a role.

Further studies are necessary to determine optimal preventative strategies in these patients.

Abbreviations
CP: Cerebral palsy; CNS: Central nervous system; DM: Diabetes mellitus; USA: United States of America; SCPE: Surveillance of Cerebral Palsy in Europe; APH: Antepartum hemorrhage; PROM: Prolonged rupture of membrane; HIE: Hypoxic-ischemic encephalopathy; CT: Computed tomography; MRI: Magnetic resonance imaging; NICU: Neonatal Intensive Care Unit; CS: Cesarean section; SPSS: Statistical package for Social Science; SD: Standard deviation; FT: Full term; PT: Preterm; ICH: Intracranial hemorrhage; MAS: Meconium aspiration syndrome; CVA: Cerebrovascular accident

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Authors’ contributions
DS wrote the paper, analyzed and interpreted the patient data regarding the disease, and performed the examination of the patient and collection of the samples. HM participate in writing and made the statistical analysis of the data. All authors read and approved the final manuscript.

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Availability of data and materials
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate
Faculty of Medicine, Mansoura University with code R20.06.859. This study was approved by the ethics committee of Faculty of Medicine, Mansoura University (Institutional Research Board (IRB) of Faculty of Medicine, Mansoura University), with approval number [R.20.06.859]. The patients’ parent provided written consent.

Consent for publication
Written parental consent had been taken, and this was approved by the ethics committee.

Competing interests
The authors declare that they have no competing interests.

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