Aetiology of cerebral palsy in children presenting at Tygerberg Hospital

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Two hundred and forty-two records of children with cerebral palsy were reviewed with regard to the aetiology of their condition. The origin of the insult was prenatal in 70 (28.9%), perinatal/neonatal in 92 (38%), acquired in 51 (21%) and unclassifiable in 29 (11.98%). Cerebral malformations (15.7%) and stroke (5.7%) were the most frequent antenatal causes, while birth asphyxia (17.3%), encephalopathy of prematurity (17.7%) and to a lesser degree kernicterus (2%) constituted the most frequent perinatal causes. Acquired cerebral palsy, particularly secondary to nervous system infections (82%), constituted a significant proportion of cases. Spastic quadriplegia (40%) was the most common type of cerebral palsy. The predominance of cases of perinatal and acquired aetiology is in contrast to the antenatal preponderance reported in developed countries.

Cerebral palsy is the most commonly occurring physical disability in childhood. Current evidence suggests that it is largely a developmental event, not significantly influenced by current obstetric technologies available in developed countries.[1] In developed countries it has been suggested that most cases of cerebral palsy occur antenatally, before the onset of labour.[2] Although cerebral palsy rates are thought to be similar in developed and developing countries,[3] the aetiology does seem to differ as the contribution of severe birth asphyxia, kernicterus and central nervous system infections (tuberculosis, bacterial meningitis, cerebral malaria) continue to be significant problems in many developing countries (Table I).[4-6] The global nature of these insults also accounts for the predominance of spastic quadriplegia in these countries. The proportion of acquired cerebral palsy cases correlates inversely with the development of a country.[7] The range varies from 5% in the most developed countries to 60% in the least developed countries.[7]

TABLE I. CLINICAL SPECTRUM OF CEREBRAL PALSY

Developed countries	Developing countries
Most cases of cerebral palsy attributable to events before labour[2,13]	Higher prevalence of postneonatal-acquired cerebral palsy cases[7] CNS infections [6,7] +++ Bilirubin toxicity [4,6] ++
Intrapartum asphyxia less than 10%[2]	Birth asphyxia [14,15] ++++
Spastic diplegia and hemiplegia the predominant types [1]	Spastic quadriplegia the predominant type [4,6]

Our objective was to identify the aetiological profile of and risk factors in children with cerebral palsy presenting to the child neurology service at Tygerberg Hospital, Western Cape.

Materials and methods

The medical records of all children with cerebral palsy at Tygerberg Children's Hospital, one of only two hospitals in the Western Cape that offers tertiary services to children, were retrospectively reviewed over a 2-year period (2003 - 2004). Variables comprised demographic, prenatal, perinatal and postnatal risk factors, investigations and co- morbidities. All children were evaluated by paediatric neurologists and/or developmental paediatricians. Confidentiality was ensured as identification details such as name or hospital number were kept in a separate, password-protected file to which only the researchers had access. The protocol was submitted to and approved by the Committee for Human Research, Faculty of Health Sciences, Stellenbosch University. Patients were excluded if the diagnosis of cerebral palsy was not definite or if the diagnosis had subsequently been changed. Other exclusion criteria included inadequate availability of data and presence of a progressive rather than static encephalopathy (e.g. HIV encephalopathy). Cerebral palsy was defined as a group of disorders of development of movement and posture, causing limitation of activity, that are attributed to non-progressive disturbances occurring in the developing fetal or infant brain (usually defined as the first 5 years of life). Demographic and family details were recorded. A Swedish classification system was used to define the type of cerebral palsy, i.e. spastic (quadriplegia, diplegia and hemiplegia), dyskinetic (choreoathetosis, dystonia), ataxic and mixed groups. A birth weight of less than 2 500 g was considered as low and delivery before 37 weeks' gestation as preterm. Infants with birth weights below the 10th percentile for gestational age were deemed to have intrauterine growth restriction (IUGR).

Encephalopathy of prematurity refers to brain injury related to prematurity and includes conditions such as intra-/periventricular haemorrhage and periventricular leukomalacia.

Birth asphyxia was diagnosed if at least 3 of the following conditions were present: (*i*) umbilical cord or early neonatal arterial pH < 7 and base deficit > 12 mmol/l; (*ii*) Apgar score < 6 for longer than 5 minutes; (*iii*) early neonatal encephalopathy with seizures; and (*iv*) other organ dysfunction (cardiovascular, gastrointestinal, pulmonary or renal system). Other identifiable causes such as trauma, coagulation disorders, infectious conditions or genetic disorders were excluded. The timing of the insult was categorised into four groups: prenatal, perinatal, postneonatal (acquired) and uncertain. Prenatal refers to the period before onset of labour, perinatal to the period shortly before or after birth, and acquired (postneonatal) to insults occurring from 28 days to 5 years of age.

Results

The medical records of 306 children with cerebral palsy were reviewed, of which 242 cases fulfilled the inclusion criteria. Male gender constituted 59% of all cerebral palsy cases. With regard to race, 74.8% of patients were of mixed ancestry, 20.9% of indigenous African ancestry, 3.73% of Caucasian ancestry and 0.4% of Asian ancestry. Nearly all patients were from socially deprived backgrounds (classified as category H1, unemployed and receiving care-dependency grants).

In patients with known gestation, preterm birth was a risk factor in 61% in the prenatal group and in 69% in the perinatal group. Regarding low birth weight (below 2 500 g) the figures were 64% and 59%, respectively.

Spastic quadriplegia (40%; *N* = 97) constituted the predominant type of cerebral palsy (Table II). The insult occurred perinatally or postnatally in the majority of patients (Table III).

TABLE II. TYPE OF CEREBRAL PALSY

	N (%)
Spastic quadriplegia	97 (40.1)
Spastic hemiplegia	64 (26.4)
Spastic diplegia	35 (14.5)
Dyskinetic	18 (7.4)
Mixed	18 (7.4)
Undetermined	6 (2.5)
Hypotonic/ataxic	4 (1.7)
Total	242 (100)

TABLE III. ORIGIN OF INSULT CAUSING CEREBRAL PALSY

	N (%)
Antenatal period	70 (28.9)
Perinatal period	92 (38.0)
Acquired	51 (21.1)
Undetermined	29 (12.0)
Total	242 (100)

The most prevalent antenatal risk factors were cerebral malformations (54.2%; *N* = 38) (Table IV). The most common cerebral malformations were disorders of histiogenesis (57%), followed by neural tube defects (18.4%), posterior fossa malformations (10.5%), and arrest of cleavage (5.2%). Absence of the corpus callosum (*N* = 12) was evident in 31.5% of patients with cerebral malformations, including 3 with neural tube defects, 2 with fetal alcohol syndrome, and 1 with chromosome 11 deletion. Stroke represented 20% of antenatal causes (*N* = 14) and univocal porencephaly was evident on neuro-imaging in 35% of patients (*N* = 5). The underlying aetiology was not identified or determined in any of the children with stroke. Cytomegalovirus (*N* = 2) and toxoplasmosis (*N* = 1) were identified in 3 children who all had severe spastic quadriplegia, with visual impairment.

Encephalopathy of prematurity (intra-/periventricular haemorrhage and periventricular leukomalacia) (46%; *N* = 43) constituted the most prevalent risk factor during the perinatal period, closely followed by hypoxic ischaemic encephalopathy (45%; *N* = 42). Dyskinetic cerebral palsy secondary to kernicterus (*N* = 5) constituted 2% of all cerebral palsy cases and 5.4% of perinatal aetiology.

Most acquired cerebral palsy cases were due to central nervous system infections such as meningitis and encephalitis (Table V). Other causes included anoxic encephalopathy after near-drowning and cerebrovascular accidents (idiopathic and severe hypernatraemic dehydration). Surprisingly, there were no cases of cerebral palsy secondary to trauma or non-accidental injury (shaken baby syndrome).

Discussion

The study investigated the epidemiology, type and causes of cerebral palsy that affect children with this condition in the Western Cape. The retrospective design of this study was a disadvantage as we were unable to obtain adequate data on a number of maternal conditions associated with

TABLE IV. MOST COMMON ANTENATAL CAUSES OF CEREBRAL PALSY

	N (%)
Cerebral malformations	38 (54.3)
Neutral tube defects	7
Arrest of cleavage	2
Disorders of histiogensis	22
Posterior fossa malformations	4
Others	3
Stroke	14 (20)
Twin pregnancy	7 (10)
Intrauterine infections	4 (5.7)
Cytomegalovirus infection	2
Toxoplasmosis	1
No organism identified	1
Fetal alcohol syndrome	4 (5.7)
Others	3 (4.3)
Total	70 (100)

an increased risk of cerebral palsy in the offspring of these patients. These data include intrauterine inflammation or chorioamnionitis, exposure to other toxins (cigarette smoke, recreational substances), documentation of placental abnormalities and histology.

Epidemiology

In this study nearly all children with cerebral palsy were from socially deprived backgrounds – consistent with other reports of children with acquired (postneonatal) cerebral palsy from elsewhere[5,6] and from Cape Town.[8] The higher prevalence was attributed to a higher occurrence of tuberculous meningitis, cerebral trauma and cerebrovascular accidents. Regarding race, Arens *et al*.[9] found that in South Africa 2.6 times more blacks than whites acquired the condition postneonatally. Although the study indicated a preponderance of male infants with cerebral palsy (59%), other studies have reported the sex-associated risk of cerebral palsy to be equal.[10]

Type

In this study the pattern of the type of cerebral palsy was similar to that seen in most developing countries[5-8] Spastic quadriplegia was the most predominant type, followed by spastic hemiplegia, spastic diplegia, and dyskinetic and mixed types of cerebral palsy.

The distribution of the clinical types of spastic cases seems to vary between developed and developing countries. Spastic quadriplegia constitutes the most prevalent type of cerebral palsy in most developing countries, whereas spastic diplegia and spastic hemiplegia predominate in some developed countries.[5-8] The higher occurrence of spastic diplegia in developed countries may be attributed to the increased survival of extreme premature infants. The high prevalence of spastic quadriplegia in developing countries reflects the contribution of severe birth asphyxia and acquired central nervous system infection.

TABLE V. CNS INFECTIONS CAUSING CEREBRAL PALSY

	N (%)
Tuberculous meningitis	23 (54.8)
Streptococcus pneumoniae	4 (9.5)
Haemophilus influenzae	2 (4.8)
Neisseria meningitidis	2 (4.8)
Group B streptococcus	1 (2.4)
Culture-negative bacterial meningitis	6 (14.3)
Herpes encephalitis	2 (4.8)
Encephalitis (no organisms identifed)	2 (4.8)
Total	42 (100)

The economic impact of cerebral palsy is enormous.

Risk factors and causes

Multiple gestations, a risk factor for cerebral palsy, contributed 10% to its prevalence in this study. This is similar to the prevalence in the USA where twins, who constitute 2% of the population, contributed 10% to the prevalence of cerebral palsy.[11]

Regarding the timing of the insult, the study identified antenatal causes in 28.9% (*N* = 70), perinatal causes in 38% (*N* = 92) and acquired causes in 21% (*N* = 51). This is in keeping with the profile found in most resource-poor developing countries.[5-8] The high proportion of perinatal cases in our study can be attributed to the large contribution of severe birth asphyxia, while central nervous system infections significantly increased the percentage of acquired cerebral palsy cases.

The most common antenatal risk causes identified in the study were cerebral malformations (54.2%) and cerebrovascular events (20%). Neuronal migration disorders were the most common type of brain malformation (see Results). Fetal alcohol exposure was identified as a risk factor in 5.7% of antenatal cases (*N* = 4). Its contribution as a cause of cerebral palsy is likely to be higher, as the use of alcohol during pregnancy is significantly under-reported. Inadequate data prevented us from exploring other toxins such as cigarette smoke and recreational drugs. Cigarette smoke predisposes the unborn infant to cerebral palsy by inducing both low birth weight and intrauterine growth retardation. Fetal methamphetamine ('tik') exposure may in future become an important risk factor, considering the alarming increase in methamphetamine abuse in the Western Cape.[12] Cytomegalovirus and toxoplasmosis were the only congenital infections implicated in the study and presented as spastic quadriplegia with blindness.

Encephalopathy of prematurity (brain injury related to prematurity) constituted the most common perinatal aetiological factor (46%), with severe birth asphyxia the second largest contributor – accounting for 45% of perinatal cases. Birth asphyxia resulting in cerebral palsy is now uncommon in developing countries.[13] Improvements in primary and obstetric care have led to less than 0.1% of newborn infants dying from birth asphyxia.[13] In developing countries, rates of birth asphyxia are several-fold higher, ranging from 4.6 per 1 000 in Cape Town to 26 per 1 000 in Nigeria.[14,15]

Kernicterus continues to be a significant problem in developing countries despite progress in the management of hyperbilirubinaemia. In a clinic-based review in Nigeria it was found that kernicterus was the most common cause of cerebral palsy,[4] while a study from India found a significant history of neonatal jaundice in 41.6% of cerebral palsy cases.[6] The incidence in the Western Cape is fortunately much lower. In this study dyskinetic cerebral palsy secondary to kernicterus constituted 2% of all cerebral palsy cases and 5.4% of those of perinatal aetiology. The recently published South African recommendations for the use of phototherapy and exchange transfusions in hospitals and primary care facilities will hopefully bring about a further reduction in cerebral palsy cases related to bilirubin toxicity.[16]

Nearly 82% of acquired cerebral palsy cases in our study were due to central nervous system infections such as meningitis and encephalitis. This is analogous to studies in other developing countries.[6,7] The large number of cerebral palsy cases due to tuberculous meningitis reflects the high (and rising) incidence rates of tuberculosis in the Western Cape and the high associated morbidity rate (50% were left with a residual disability) coupled with young age of presentation.

Conclusion

The aetiological profile of the study confirms that the clinical spectrum of cerebral palsy in the Western Cape is consistent with that described in other developing countries.

Our observation that five categories of aetiology (cerebral malformations, stroke, encephalopathy of prematurity, severe birth asphyxia and central nervous system infections) are responsible for the majority of all observed causes of cerebral palsies identified suggests that emphasis should be placed on strategies of prevention, intervention and treatment. The economic impact of cerebral palsy is enormous. Targeting preventable causes may help to reduce the burden of childhood disability in South Africa.

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