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CEREBRAL PALSY IN CHILDREN: SUBTYPES, MOTOR FUNCTION AND ASSOCIATED IMPAIRMENTS; ADDIS ABABA, ETHIOPIA

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Abstract

Background:

Cerebral Palsy is one of the most common developmental disabilities among children seeking health care services in Ethiopia as well as in other low income countries. Yet, there is no national data relating to CP in Ethiopia. The overall aim of this study is to describe the clinical subtype, gross and fine motor function and presence and pattern of associated impairments and possible risk factors in children with Cerebral Palsy aged 2 to 18 years in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

Methods: A hospital based descriptive cross-sectional study conducted among 207 children with Cerebral Palsy. Surveillance for Cerebral Palsy in Europe (SCPE) decision tree was used to include 174 illegible children then a pretested and pre-coded questionnaire administered to caregivers assessing socio demographic characteristics, associated impairments and possible risk factors; evaluated with proper neurologic examination to classify them; and severity of gross and fine motor impairment was assessed by evaluating level of function by grading according to GMFCS and MACS. The IBM SPSS V.21 was used for data analysis, and a significance level of 0.05 was chosen.

Result: A total of 174 children who fulfilled the clinical criteria were included sampled consecutively. Mean age 5.6 (SD 3.6) year; Males 55.2%. Under five children were 50.6%. Majority of the children had Bilateral spastic CP (60.4%) followed by unilateral spastic CP 21.8%, Dyskinetic CP 10.4%, Ataxic CP 3.4% and 4% were unclassifiable. Of all the children 95.4% had speech and language impairments, 87.4% learning disabilities; 60.9% epilepsy, 24.7% Visual impairment and 8.6% has hearing impairment. On gross motor functions and manual ability assessment 75.3% of the children had level 4 and 5 functional impairment. More than 80% of the mothers had complications during delivery (fetal distress followed by PROM). Half of the neonates did not cry immediately after birth; 77 neonates were resuscitated with BMV at birth and 111 immediately admitted to NICU. Subsequently during the first month of life; 50% had infection, 62% trouble feeding, 49.4 % difficulty breathing, 35% seizure and 13.8% had deep jaundice.

Conclusion; the severe forms of CP prevail and most children are dependent on their parents for routine activities and cannot communicate well. Multidisciplinary care approach and focused functional rehabilitation services need to be instituted. Causal relationship cannot be drawn from this study but makes a strong argument for improving maternal and child health care.

Key Words: Cerebral Palsy; children; subtypes; impairments; motor function; Ethiopia

Background

Cerebral Palsy (CP) is one of the most common developmental disabilities among children seeking health care services in Ethiopia as well as in other low and middle income countries (LMIC). Yet, it was not included in a recent report on the Global Burden of Disease of Developmental Disabilities.¹ One reason for this omission, is probably the lack of robust population based studies in Africa and other LMIC. Until recently there were only studies on clinical samples suggesting a wide range of prevalence estimates from 2-10 cases per 1000 children²⁻⁵. During recent years, a couple of rigorous population based studies have been published from Uganda⁶ and Bangladesh⁷ revealing large discrepancies compared with prevalence data from HIC⁸. The Ugandan and Bangladesh studies showed higher prevalence of CP 2.9/3.4 per 1000 children, compared to about 2 per 1000 in HIC. In fact, during the first years of life the prevalence was even higher, declining over time by a high premature mortality after the first years⁶. In addition to having a higher prevalence, the etiological risk factors differed in Uganda, with almost no preterm born children (compared to <40% in HIC), and numerous cases due to post neonatal infections (e.g., malaria). These studies clearly show the need of studies on CP from LMIC and that information cannot be extrapolated from studies in HIC.

A population based study in Uganda revealed that Children with CP in Uganda lack access to health care, Assistive devices, and education, which probably contributes to their poor development of mobility and self-care skills⁹. A national survey on children with disabilities in Ethiopia suggests that the vast majority are not in school, and anecdotal evidence suggests many do not have access to community-based rehabilitation^{10, 11}. However, the prevalence of children and adults with disability, including CP, is not known in Ethiopia, and there is no studies describing the clinical and socio demographic panorama of children with CP. It is not known what subtypes of CP are present, the level of motor function these children exhibit, or the presence of risk factors causing the disorder. The aim of this study was to describe clinical subtypes, motor impairments and associated impairments and risk factors using comprehensive methodology and terminology of a clinical cohort of children with CP at the University Hospital in Addis Ababa, the capital of Ethiopia. The results will increase our knowledge on the situation of CP in Ethiopia, and serve as a basis for setting up larger epidemiological and community-based intervention studies to improve the quality of life of children with CP and their caregivers in Ethiopia.

Methods

Study Setting

This was a prospective, hospital based, descriptive cross-sectional study conducted July-September 2018, at the Pediatrics Neurology Outpatient Clinic in Tikur Anbessa Specialized Hospital (TASH), Department of Pediatrics and Child Health, Addis Ababa. TASH is the largest teaching referral hospital in Ethiopia with over 700 beds. About 500-700 children visit the Pediatrics Neurology Outpatient Clinic every month; of these 25-30% have cerebral palsy; two third of the patients are from Addis Ababa and the rest are referred from countryside with the majority coming from Oromia region.

Participants and procedures

A total of 174 children in the age span 2 - 18 years with confirmed diagnosis of CP were included in the study. They were recruited from a total of 207 children from two groups with suspect motor symptoms. In the first group, 31 children were searching the neurological outpatient clinic for the first time, and in the second group, we re-examined 176 children who had earlier visited the clinic and been diagnosed with CP by less stringent diagnostic procedures.

The assessments were conducted in a series of three steps performed by the principal investigator (ST) and two General Practitioners (GP). In the first step, ST screened all children in both groups using targeted history, physical examination and chart review. Children with obstructive hydrocephalus ($n = 2$), extra cerebral birth defects ($n = 2$), progressive motor disorder ($n = 11$), muscle hypotonia ($n = 7$) or presence of an isolated spinal neural tube defect ($n = 3$) were excluded. In total 25 children, 11 from first group and 14 from the second group, were excluded.

In the second step, 182 children (20 from the first group and 162 from the second group) were examined by the GPs according to the SCPE decision tree⁸. All 20 children from the first group were confirmed to have CP, while 8 children from the second group, did not fulfill the criteria for CP. Among the eight who were excluded, three had only posture or movement abnormalities but no motor function abnormality, four had loss of previously acquired skills, and one had generalized muscle hypotonia without symptoms of ataxia.

In the third step, the 174 children with confirmed CP included in the study population were assessed by structured questionnaire and neurologic examination with the tools described below and classified to sub-type CP⁸. The above stated procedures and steps followed based on the SCPE decision tree to select the study participants is clearly outlined on **Figure 1**.

1. Socio demographic

The GPs used a pretested and pre-coded questionnaire to interview the caregivers. Questions include the child's age, sex, level of education, medical history from pregnancy to the present, family history, the

child's developmental milestones, past and present nutritional history, parental educational status, living condition and family history of illness.

2. General Clinical Examination

A standard neurological examination including assessment of motor impairment was performed by the GPs advised by pediatric neurologist (AM) and ST.

3. Functional Assessment

Gross and fine motor functions were assessed and classified according to the GMFCS and MACS by the GPs. These classification systems grade the motor impairments from mild to severe in a 5 level Likert scale, where Level I indicates mild limitations and V severe impairments.

4. Associated impairments

Information of associated impairments were collected by structured interviews with the caregiver using a protocol based on the UNICEF/ Washington group Child functioning module. The associated impairments assessed for included Intellectual disability, Behavioral abnormalities, Speech difficulties, Feeding difficulties, Visual impairment and Hearing impairment and seizures (see supplement info for details).

5. Risk factors

Information on prenatal, perinatal and postnatal risk factors were assessed using structured questionnaires administered to caregivers. The questions addressed any complications during the antenatal period such as maternal infections and drug intake, as well as gestational age, place of delivery, birth weight, and complications during delivery, neonatal resuscitation, neonatal admissions and medical history during the first 2 years of life.

Quality control; The principal investigator daily checked for completeness of data collection, verified physical examination finding and classification of subtype of CP for each child.

Data analysis

After data cleaning and entry, analysis was done using the Statistical Package for Social Sciences (SPSS) version 21 by an employed biostatistician. Data cleaning and entry was also done manually by the principal investigator and cross checked with the entered data by the biostatistician. The data was analyzed using descriptive statistics and the statistical significance was tested using chi square. P value less than 0.05 was considered as statistically significant. Bivariate analysis was done to see crude association followed by multivariate analysis for significantly associated factors.

Results

Clinical subtypes and severity of gross and fine motor impairments

Bilateral spastic CP was the predominant subtype (60.4%) followed by Unilateral spastic CP (21.8%), Dyskinetic CP (10.4%), Ataxic CP (3.4%) and unclassifiable CP (4%). Among children with bilateral spastic CP, 88 children (84%) had quadriplegic. Left sided involvement was predominant among children with unilateral spastic CP.

The distribution among GMFCS and MACS levels severity of the motor function impairments are shown in **Table 1**. A majority of children presented with severe impairments in both gross motor (75% at GMFCS level IV-V) and fine motor functions (75% at MACS level IV-V). Only 14% had the milder levels (I-II) of impairments.

Associated Impairments

The prevalence of the recorded associated impairments is shown in **table 2**. Each child had at least one associated impairment and 30 children had two and 144 three or more. Speech difficulties (95%) and intellectual disability (87%) were most common. Seizure was present in 61% of the children, and of these 85% had been medicated with anticonvulsant, and 90% had been taken to the “holy water” (traditional healing spiritual water) at least one time. Seizure was also the most common cause of admission to hospital. Visual and hearing impairments were less prevalent, yet quite common, 24.7% and 8.6%, respectively. All children with visual or hearing impairments were sent to specialist, and 20.7% and 4.6%, respectively were confirmed. The remaining children did not show up at their appointed time.

The statistical analysis revealed association between sub-type, GMFCS and MACS severity levels and some associated impairments. There was a strong correlation between speech/language impairment (P-value – 0.007) and the subtype of CP (P-value – 0.001). Multivariate analysis showed that children with language impairment were 11.5 times more likely to be at GMFCS level IV-V compared with those without language impairment. Children with bilateral spastic CP were 3 times more likely to have GMFCS IV-V, compared to other subtypes. Bivariate analysis, showed a correlation between speech and language impairment, visual impairment and GMFCS and MACS levels. However, on multivariate analysis, the only association that remained with statistical significance was the association between GMFCS and MACS. The subtypes of CP were not associated with MACS levels.

Perinatal risk factors

Information about the antenatal, perinatal and postnatal period is presented in **table 3**. There were little remarkable events during the antenatal care: In more than half of the mothers the duration of labor was less than 24 hours. Notably, less than 10 % of the children in this CP cohort were born preterm and none had a birth weight below 1000g.

However 95% of the mothers had complications during delivery identified as fetal distress (42.7%) followed by prolonged rupture of membrane (PROM) (25.9%). Almost two thirds of the children had been admitted to the NICU; most common cause of admission was respiratory distress (76.6%) and infection (11.7%). In the postnatal period, 54% of the neonates had infection (4.2% meningitis and 3.2% tetanus), 62% had trouble feeding, 49.4 % had difficulty breathing, 35% had seizure and 13.8% had deep jaundice with acute bilirubin encephalopathy.

The Bivariate analysis of perinatal factors, showed that the presence of fetal distress and PROM were associated with higher frequency of spastic cerebral palsy subtypes, whereas precipitated labor was associated with higher frequency of dyskinetic or ataxic forms of cerebral palsy. The requirement for bag mask ventilation was associated with higher prevalence of spastic cerebral palsy. The presence of seizure in the neonatal age was more common in spastic cerebral palsy, while deep jaundice was associated with higher prevalence of dyskinetic/ataxic subtypes. There was no association identified between the perinatal factors and the motor function impairment severity level. The multivariate analysis is shown on **table 4**.

Sociodemographic characteristics

Details of sociodemographic characteristics is presented on **Table 5**; The mean age of the 174 children in the CP cohort was 5.6 (SD 3.6) years with male predominance. Seventy percent of the children above 5 years did not attend school, and among those who attended one third performed on the last ten ranks in the respective classroom and 20% had repeated a grade. Mothers alone were the primary care givers in 24.7% of the children, 56.9% of children were being cared by both parents (mothers being the primary caregivers supported by fathers). Majority of the mothers (70.4%) were house wives.

Discussion

This clinical cohort of children with confirmed CP diagnosis from the main tertiary hospital in Ethiopia included a large majority of severely motor impaired children with associated impairments and seizures. In most children, one or several perinatal risk factors were identified, unmasking the potential to prevent

the brain injury if properly treated. A majority of children did not attend school but was cared for by the mothers working as house wives.

Comparison with other clinical and population based cohorts

The clinical profile of this cohort differs from recent population based cohorts of children with CP in Uganda⁶ and Bangladesh⁷. We found that 75% of children had severe motor impairments at GMFCS or MACS level IV-V, while children with such severe impairments ranged between 36-48 % in the Ugandan and Bangladesh cohorts, and 32-33% in population cohorts from HIC^{8,12}. In our cohort, we found few children with mild impairments (GMFCS level I-II, which was prevalent particularly among the older children in the Ugandan cohort. The high proportion of children with severe impairments are more in par with other clinical cohorts from Uganda, Egypt ^{4,5,13,14,15}, North India¹⁶. Many of the children suffered from seizures (61%), and had probably been identified when seeking to get anti-convulsing drugs.

The rate of speech and language impairment in our study differed largely from other African studies and approximates to an Indian study (83.7%)^{17, 18}. The high rate was found to be associated with the severity of motor function in our study. It may also be attributed to the lower rate of attending school and higher rate of cognitive impairment. In a Sweden study, it was shown that communication function correlates to gross and fine motor and cognitive function and children with severe form of CP found to have lower communication function level¹⁹.

The high numbers of severe (quadriplegic) bilateral spastic type of CP suggests injuries to the full term brain due to complications during the birth process such as birth asphyxia or acquired central nervous system infections such as meningitis or encephalitis⁴. The lower frequencies of milder levels of bilateral (diplegic) spastic type of CP suggests injuries to the preterm brain and may reflect less recruitment from children born preterm similar to the findings in Uganda⁶ and contrary to the Australian study where 43% of children with CP were born preterm¹². Probably, children born preterm do not survive the neonatal period due to complications during the first neonatal weeks and limited support from the maternal/newborn health care service provided²⁰. This is supported by only few preterm born children in this study, no one with Extremely Low Birth Weight.

On assessment of perinatal factors, we identified that those children with spastic subtype of CP had higher rate of fetal distress and PROM during the perinatal period, higher rate of language and speech difficulty and worse functional impairment while those with Dyskinetic and Ataxic CP were found to have higher rate of precipitated labor and deep jaundice during the neonatal period. These findings may indicate that spastic subtype of cerebral palsy may be associated with perinatal hypoxic insult as in cases of fetal distress, while dyskinetic and ataxic forms may be associated with bleeding and injuries to the deep grey matters of the brain that can occur in cases of precipitated labor²⁰. However, due to the fact that the

possible causes were identified based on history given by the parents (no registries available nor MRI results) causal relationship of definitive risk factors cannot be determined based on this study.

By applying stricter criteria and procedures for setting the diagnosis CP we found that 22 children of the 176 children who had been given the diagnosis at an earlier visit to the clinic, did not fulfill the SCPE criteria. We also changed the subtype of 20 children following proper evaluation. Over the years the criteria for the CP diagnose including different subtypes has developed and the newer definition²¹ is now used in most HIC. In combination with functional classifications systems for gross and fine motor, and communication, it provides a detailed description of the child which is very useful in clinical practice for planning interventions and for predicting prognosis. It is also very useful in research when comparing different cohorts of children, e.g., from different countries. Previously older systems have been used in Ethiopia, and probably in many countries in sub-Saharan Africa and other LMIC. A previous retrospective study from our hospital TASH showed 48.2% of unclassified CP²², which differs significantly from the present study. The prospective assessment of the children in this study provided high-quality clinical information that could be systematized. Hopefully, this study, and studies from other countries in sub-Saharan Africa, can pave the wave for this contemporary method to set diagnose and functional limitations, which would also lead to a change to better clinical practice.

Strengths and limitations.

A strength in this study was the prospective study design using the contemporary international system for setting CP diagnose and severity level of motor impairments and assessing associated impairments, making it possible to compare with other cohorts. The sample was also large enough to perform some statistical analyses, however, causal relationships cannot be determined from our study as it was a cross

sectional study done at a point in time. We took a cut off age at 2 years while the SCPE recommends 4. We are confident on the diagnosis of CP but the subtypes might change with time.

A major limitation was that the sample was not representative for the general population but derived from a clinical cohort, in which families had actively searched for services leading to a bias towards more severe forms. Another limitation was that much of the information on risk factors and associated impairments were based on interviews and surveys of the caregivers which were prone to recall bias.

Conclusion

Most of the children in our study had severe functional impairments and were dependent on the caregivers for their daily living. This is a hard burden on the care givers in addition to the frustration having no access to rehabilitation services. Proper diagnosis, categorizing into the clinical subtypes, assessing motor function and co morbidities are essential for early intervention and follow-up. The study also find that many children had adverse events during the perinatal period, which could be preventable and call for improved maternal and neonatal care. Overall, the efficient management of these children will require a multidisciplinary care team to obtain the best care of their medical and psychosocial needs and following the ICF frame work²⁵.

Abbreviations

AAU;Addis Ababa University, CHS;College of Health Science, CP;Cerebral Palsy, GDD;Global Developmental Delay,GMFC;Gross Motor Functional Classification, HIC;High Income Countries, ICF;International Classification of Functioning, Disability and Health, LMIC;Low and Middle Income Countries, PROM;premature Rupture Of Membrane,PNC; Pediatrics Neurology Clinic , SCPE;surveillance of Cerebral Palsy in Europe, TASH;TikurAnbessa Specialized Hospital

Declarations

Ethical approval and consent

Ethical clearance was obtained from IRB of Pediatrics and Child Health Department's Research and Publications Committee of the School of Medicine, CHS and AAU and all methods were performed in accordance with the relevant guidelines and regulations. Respondents were clearly informed about the purpose of the study and the information required from them. Informed, written consents from primary care takers (parents/guardians) were obtained. Personal identifiers like name of participants were not used to maintain confidentiality. All participants included in the study are kept anonymous during subsequent analysis and dissemination. Children with unaddressed associated impairment diagnosed during the study were linked to the respective specialty evaluation and management.

Consent for Publication; Not applicable.

Availability of data and materials;

The data sets used and/ analyzed during this study are available from the corresponding author on reasonable request.

Competing interests;

The authors declare that they have no competing interests.

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Authors' contribution;

ST designed the study, extracted the data, provided oversight of field work and data quality control, interpreted the analysis and finally drafted and wrote the manuscript. HF arranged a visit to Ethiopia to organize the set of data that was collected and he convinced the neuropaediatric unit at Karolinska Institute to fund the research. He was in fact was the basis for ST to pick the research topic seeing what he and his group did at Uganda. Ayalew M organized the pediatrics neurology clinic staff for the data collection and provided confirmatory diagnosis in doubtful cases. HF and Amha M contributed to the design and conceptualization of the study; provided critical input at each report and finding, participated in drafting and improving the manuscript and reviewed the final manuscript as submitted. WA participated on designing the study and reviewing the first report and also helped in the printing of all of the questionnaires used to collect the data. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Figures

Figure 1

the process undertaken to select the final participants on the study. Among the initial 207 patients, 174 were included on the final study after excluding the rest based on the SCPE decision tree (Surveillance of cerebral palsy in Europe: a collaboration of Cerebral palsy surveys and registers. Dev Med Child Neurol. 2000; 42:816–24) depicted above.

Supplementary Files

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