Contribution of perinatal conditions to cerebral palsy in Uganda

Worldwide, an estimated 93 million children are disabled, 80% of whom live in low-income countries.[1] Cohort studies in high-income countries attribute more than 50% of cerebral palsy cases to premature birth or prenatal causes.[2] Equivalent data have been difficult to obtain in low-resource settings, limiting the ability to lobby for better service provision for these children.

In October, 2017, Angelina Kakooza-Mwesige and colleagues[3] published the largest population-based study of cerebral palsy in sub-Saharan Africa. This important work highlighted the higher prevalence of cerebral palsy in children in sub-Saharan Africa than in children in high-income countries, and that a greater proportion of cases are from potentially preventable causes. However, for diagnostic precision, consistent with all major international cerebral palsy registers, children younger than 2 years were not included. We suggest that further exploration of this younger group is important given the high proportion of full-term neonatal cases with severe cerebral palsy identified in this setting.

We wish to add our experience of this important younger subgroup in an urban hospital setting in Kampala, Uganda. We investigated the causes and subtypes of cerebral palsy in 130 children younger than 18 years who presented to Mulago National Referral Hospital—the largest paediatric centre in Uganda—over an 8 week period in 2013. Children younger than 2 years were not excluded because of concern that those with severe cerebral palsy might not survive beyond early childhood. Children in whom there was concern about movement or posture were identified by doctors and therapists working in the paediatric in-patient wards and neurology, physiotherapy, and occupational therapy clinics. Children were recruited and assessed by the study lead (JH) or a local paediatrician trained in cerebral palsy assessment, assisted by a local language (Luganda) translator. Written consent was obtained. Cerebral palsy diagnosis was confirmed in cases of onset of non-progressive movement disorder before age 2 years. Children with neural tube defects or isolated hypotonia were excluded.

Assessment involved obtaining detailed retrospective histories from primary caregivers, including any self-identified antecedents to the onset of motor impairment, and neurological examination. Cerebral palsy subtype was assigned according to the Surveillance of Cerebral Palsy in Europe hierarchical classification. Neuroimaging was not available.

In this hospital-based cohort, 56% of patients were male, 9% were in-patients, and 63% were younger than 2 years (median age 17 months [IQR 9–29]). 78% of patients had bilateral spastic disease; 72% had four-limb spastic disease resulting in severe functional impairment. 68% of caregivers gave histories consistent with term intrapartum-related encephalopathy or neonatal sepsis, and 76% attributed their child's cerebral palsy to severe (full-term) neonatal illness, supported by a history of admission to neonatal care facilities (table). Two children were HIV positive.

Key differences exist between our urban hospital-based cohort and the predominantly rural population-based cohort reported by Kakooza-Mwesige and colleagues.[3] Our cohort was younger (median age 17 months *vs* 4–5 years), with more cases of four-limb cerebral palsy, suggesting a higher prevalence of global brain injury that usually results from intrapartum or neonatal complications, as opposed to less disabling unilateral lesions.

The younger age of patients and greater severity of disease seen in our hospital cohort might reflect increased care seeking or referral for these patients, as well as an increased incidence of comorbidities (eg, infection, malnutrition) precipitating

	Total (n=130)	Subtype of cerebral palsy		
		Bilateral spastic (n=101)	Unilateral spastic (n=15)	Dyskinetic (n=14)
Premature birth (<37 weeks)	8 (6%)	8/8 (100%)	0/8 (0%)	0/8 (0%)
Term neonatal illness	99 (76%)	..	..	..
Intrapartum-related encephalopathy, with or without infection	75 (58%)	66/75 (88%)	5/75 (7%)	4/75 (5%)
Neonatal sepsis, with no evidence of encephalopathy	14 (11%)	13/14 (93%)	1/14 (7%)	0/14 (0%)
Neonatal jaundice	7 (5%)	0/7 (0%)	0/7 (0%)	7/7 (100%)
Other neonatal illness	3 (2%)	1/3 (33%)	2/3 (67%)	0/3 (0%)
Post-neonatal event	14 (11%)	..	..	..
CNS infection	12 (9%)	9/12 (75%)	2/12 (17%)	1/12 (8%)
Other	2 (2%)	0/2 (0%)	2/2 (100%)	0/2 (0%)
Unknown	9 (7%)	4/9 (44%)	3/9 (33%)	2/9 (22%)

Data are n (%) or n/N (%).

Table: **Attributed causes of cerebral palsy**

hospital attendance. In another Mulago Hospital-based study of cerebral palsy, also by Kakooza-Mwesige and colleagues,[4] children older than 2 years recruited from the cerebral palsy outpatient service (n=135) were also younger (median age 3·5 years) and more had severe impairment (39% *vs* 20%) than in the recent population-based study.[3]

Difficulty confirming cerebral palsy subtype in children younger than 2 years might have affected our findings; neurodisability from severe brain injury is often apparent early, whereas milder impairments might be missed. The lower proportion of bilateral spastic disease in Kakooza-Mwesige and colleagues' hospital-based cohort[4] than in our cohort (46% *vs* 78%) might be explained by our inclusion of patients younger than 2 years and of in-patients, potentially with cerebral palsy-related comorbidities. However, the population-based study[3] also showed a trend towards increased cerebral palsy prevalence and severity in younger children. The very high proportion of severely disabled young children in our hospital-based cohort indicates an increased early morbidity and mortality. Therefore, studies excluding young children might underestimate the preventable burden of severe neurodisability.

Importantly, 73% of Kakooza-Mwesige and colleagues' population-based cohort[3] were neonatal full-term cases; however, no further perinatal history was given. Our study suggests that intrapartum-related encephalopathy and sepsis are key contributors to this cerebral palsy burden and that severe cases attributed to these causes might die before reaching age 2 years, when they can be included in cerebral palsy registries.

Newborn deaths due to premature birth, intrapartum-related events, and sepsis account for almost half of under-5 mortality worldwide,[5] with a high estimated burden of adverse neurodevelopmental outcomes in survivors.[6,7,8] Together, these studies emphasise the substantial burden of severe neurodisability attributable to term neonatal morbidity. Intrapartum and newborn care must remain key priorities to ensure all children can survive and thrive.

We declare no competing interests.

Jane Hassell, Cally Tann, Richard Idro, Nicola J Robertson
jane.hassell@ucl.ac.uk

University College London, London, UK (JH, CT, NJR); London School of Hygiene and Tropical Medicine, London, UK (CT); Makerere University College of Health Sciences, Kampala, Uganda (RI); and Sidra Medicine, Doha, Qatar (NJR)

1 WHO. World report on disability. 2011. http://www.who.int/disabilities/world_report/2011/report.pdf (accessed Dec 10, 2017).
2 Himmelmann K, Uvebrant P. The panorama of cerebral palsy in Sweden. XI. Changing patterns in the birth-year period 2003–06. *Acta Paediatr* 2014; **103:** 618–24.
3 Kakooza-Mwesige A, Andrews C, Peterson S, Wabwire Mangen F, Eliasson AC, Forssberg H. Prevalence of cerebral palsy in Uganda: a population-based study. *Lancet Glob Health* 2017; **5:** e1275–82.
4 Kakooza-Mwesige A, Forssberg H, Eliasson AC, Tumwine JK. Cerebral palsy in children in Kampala, Uganda: clinical subtypes, motor function and comorbidities. *BMC Res Notes* 2015; **8:** 166.
5 Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. *Lancet* 2016; **388:** 3027–35.
6 Blencowe H, Lee AC, Cousens S, et al. Preterm birth-associated neurodevelopmental impairment estimates at regional and global levels for 2010. *Pediatr Res* 2013; **74** (suppl 1)**:** 17–34.
7 Lee AC, Kozuki N, Blencowe H, et al. Intrapartum-related neonatal encephalopathy incidence and impairment at regional and global levels for 2010 with trends from 1990. *Pediatr Res* 2013; **74** (suppl 1)**:** 50–72.
8 Kohli-Lynch M, Russel NJ, Seale AC, et al. Neurodevelopmental impairment in children after group B streptococcal disease worldwide: systematic review and meta-analyses. *Clin Infect Dis* 2017; **65:** S190–99.