

Gross Motor Dysfunction in Children with Cerebral Palsy in Bauchi, North-East Nigeria

Authors: I. A. Adedeji^{1,2,*}; M. F. Bashir^{1,2}; A. S. Adamu^{1,2}; K. Shuaibu²; A.M. Jibrin²

Affiliations:¹Department of Pediatrics, Abubakar Tafawa Balewa University; ²Department of Pediatrics, Abubakar Tafawa Balewa University Teaching Hospital

ABSTRACT

INTRODUCTION: Cerebral palsy (CP) is a common childhood neurological disorder with the hallmark of varying degrees of impaired motor function. Identifying the factors that influence children's motor outcomes with CP will lead to a more informed treatment and prognostication approach.

METHODS: This was a cross-sectional cohort study involving 70 consecutively enrolled children with CP. Information on socio-demographic background and risks for developing CP was obtained. The children were assessed for common CP-related comorbidities, gross motor function was evaluated with the aid of GMFCS-E&R, and the clinical subtypes of CP were recorded. The data were analyzed using IBM SPSS Statistics V21.

RESULTS: The subjects' mean age was 49 months, and most (40%) were from the lower socio-economic cadre. The majority (44.3%) were at GMFCS level V and 62.9% were non-ambulatory. The odds of having non-ambulatory CP were higher among children with quadriplegic CP ($p=0.000$, $CI=0.010-0.228$, $OR=0.048$) and those who had jaundice as a risk factor (p value= 0.038 , $CI=0.118-0.961$, $OR=0.336$). Whereas, the presence of a single risk factor, as opposed to multiple risk factors, was associated with higher odds of being ambulatory ($p=0.028$, $CI=1.113-10.702$, $OR=3.451$).

CONCLUSION: The exposure to multiple adverse factors at birth and early neonatal life may explain why most of the children with CP in this study were non-ambulatory. This calls for improvement in the spread and quality of intrapartum and early neo-natal care. Furthermore, we have demonstrated the link between topographical subtype and ambulatory potentials, which may have far-reaching counseling and prognostic value.

Keywords: Cerebral Palsy, Gross Motor Function, Comorbidities, Risk Factors

INTRODUCTION

Cerebral palsy (CP) is a movement and posture dysfunction that results from non-progressive damage to a developing brain [1]. It is one of the most common disorders seen at pediatric neurology outpatient services across Nigeria and many other sub-Saharan Africa [2-4]. This suggests that conditions that predispose individuals to adverse neurological sequelae, such as CP, are still prevalent in this region. Previous studies have established perinatal asphyxia, neonatal jaundice and intracranial infections as the most frequently encountered risks for developing CP in Nigeria [5,6]. However, motor impairment remains a major management concern for many children with CP. This varies widely

in its manifestation, degree of limitation of movement and subsequent need for ambulatory support.

The Gross Motor Function Classification System (GMFCS) is a task-oriented 5-level classification method that reliably describes the motor function of individuals with CP [7]. It focuses on self-initiated movement and the requirement for ambulatory aid. The mildest stage (level I) implies that the individual can perform usual activities, albeit with reduced speed and coordination. In contrast, at level V, movement is severely restricted and powered mobility devices are required [7]. Generally, individuals who belong to levels I and II do not require mobility aids, whereas there is a progressive advancement in the requirement for aids from levels III to V [7]. Thus, beyond providing a clear picture of the motor function,

*Corresponding author: I. A. Adedeji, Abubakar Tafawa Balewa University Teaching Hospital, Bauchi, Nigeria, Department of Pediatrics, Abubakar Tafawa Balewa University Teaching Hospital, Bauchi, Nigeria. Email: adedejidris@yahoo.com. Phone: +2348033661132; **Potential Conflicts of Interest (Col):** All authors: no potential conflicts of interest disclosed; **Funding:** All authors: no funding was dis-closed; **Academic Integrity.** All authors confirm that they have made substantial academic contributions to this manuscript as defined by the ICMJE; **Ethics of human subject participation:** The study was approved by the local Institutional Review Board. Informed consent was sought and gained where applicable; **Originality:** All authors: this manuscript is original has not been published elsewhere; **Type-editor:** Himani (USA)
Review: This manuscript was peer-reviewed by three reviewers in a double-blind review process;
Received: 11th November 2019; **Initial decision given:** 26th January 2020; **Revised manuscript received:** 12th July 2020; **Accepted:** 08th September 2020.

Copyright: © The Author(s). This is an Open Access article distributed under the terms of the Creative Commons Attribution License (CC BY-NC-ND) (click here) which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. **Publisher:** Rwanda Biomedical Centre (RBC)/Rwanda Health Communication Center, P.O.Box 4586, Kigali.
ISSN: 2079-097X (print); 2410-8626 (online)

Citation for this article: I. A. Adedeji; M. F. Bashir; A. S. Adamu et al. Gross motor dysfunction in children with cerebral palsy in Bauchi, North-East Nigeria. Rwanda Medical Journal, Vol. 77, no. 4, pp. 14-19, 2020.

GMFCS also gives an idea of the mobility aid or equipment an individual with CP will require.

Gross motor function has been observed to have some association with the CP's physiological and topographical type. Children with spastic quadriplegia tend to have less functional levels of GMFCS (levels IV and V) [8]. Furthermore, malnutrition, the etiology of CP, and the presence of co-existing neurological impairment are all factors that have been linked to the severity of impairment in motor function [9,10]. An adequate understanding of the patterns of motor impairment and comprehensive profiling of their correlates may contribute to an improved and more informed approach towards prioritizing and deploying resources in managing children with CP. However, such detailed information on the motor function of children with CP in many parts of sub-Saharan Africa, especially in Northern Nigeria, remains very sparse.

This study aimed to describe gross motor impairment and its correlates among children with CP at the pediatric neurology clinic of Abubakar Tafawa Balewa University Teaching Hospital, Bauchi (ATBUTH). The study hypothesized that there is a relationship between motor impairment and the risk factors for developing CP. The study further assumed that CP-related co-morbidities and the physiological forms of CP affect the GMFC level.

METHODS

This cross-sectional cohort study was carried out at the pediatric neurology clinic, ATBUTH, following approval by the Research and Ethics Committee (Ref: REC0018/20). A total of 70 subjects between the ages of 7 months and 18 years who came for their routine follow-up visits for CP were enrolled in the study after informed consent was obtained from the parents. The enrolled adolescents had some degree of learning impairment; hence, assent could not be accepted. Subjects were recruited between June 2018 and February 2019. Within this period, all the children who were being followed up for CP at the child neurology clinic and eligible were enrolled in the study. Children with other forms of movement or motor disability that did not fit into the CP's definition were excluded. The diagnosis of CP was made by a Consultant Paediatrician and two Paediatrics Trainees.

A semi-structured questionnaire was used to obtain information on socio-demographic background, risk factors for and co-morbidities of CP. The method recommended by Olusanya was utilized in classifying the socio-economic status (SES) of the parents. In contrast, the gross motor function was classified with the Gross Motor Function Classification System's aidstem, Expanded and Revised (GMFCS-E&R®) [11]. The topographical and physiological classifications of CP were also done. The GMFCS was grouped into ambulatory (levels I, II & III) and non-ambulatory (levels IV & V). The parents' SES was classified into the upper, middle and lower classes based on the recommendation by Olusanya et al. [11]. Risk factors and co-morbidities of CP were further grouped into a classification of either single or multiple factors.

Questions were asked from the parents/caregivers about the presence of perceived visual or speech impairment. The vision was further assessed by finger counting and light perception,

while appropriateness of the children's speech for their ages was also evaluated. [12] Children who had deficits in two of the following areas were adjudged to have impaired adaptive behavior. This was used as a proxy for intellectual impairment in our study. The areas were: communication, self-care, home living, social/interpersonal skills, community resources, self-direction, functional academic skills, work, leisure, health, and safety [13].

All data generated were processed and analyzed using IBM SPSS Statistics V 21®. The chi-square and Fisher's exact tests were used to establish the association between categorical variables. The statistical significance level was < 0.05, at a confidence interval (CI) of 95%.

RESULTS

Socio-economic background

A total of 70 children with a diagnosis of CP were recruited into this study. The subjects had a mean age of 49 months, and most (40%) had parents that belonged to the lower socio-economic class

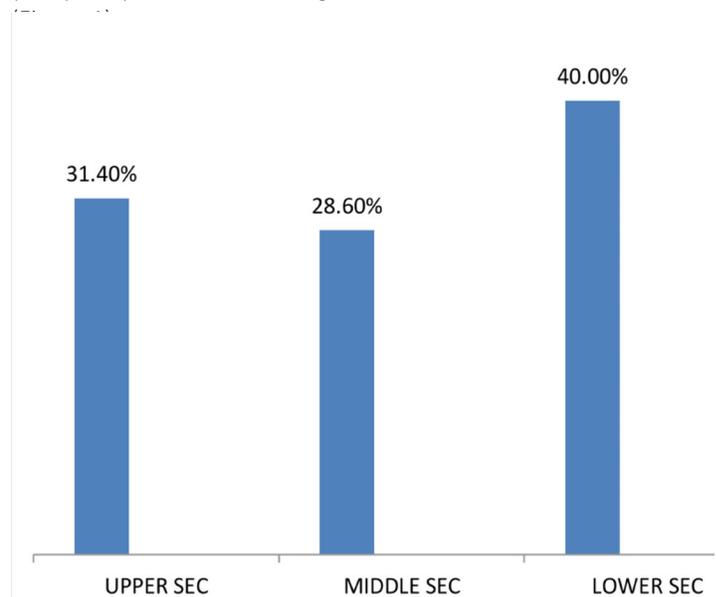


Figure 1: Socio-economic status of subjects

SEC: Socio-economic class

GMFCS and sub-classification into ambulatory and non-ambulatory CP

The severest level of gross motor impairment (class V) was the most frequently observed in this study, accounting for 44.3% of the study participants. GMFCS classes I and II constituted 17.1% each, while 8 (11.4%) and 7 (10%) of the children were at levels III and IV. (Figure 2). Overall, the majority of the children were found to have non-ambulatory CP (GMFCS classes III, IV and V), while ambulatory CP (classes I and II) constituted 37.1% (Figures 3).

Relationship between GMFCS and socio-economic class (SEC)

Most of the children observed to have Ambulatory CP were from the lower SEC. Among those with Nonambulatory CP, 34.1% were each from the upper and the lower SEC, while 31.8% were from the lower SEC. This study did not show a significant relationship between parents' socio-economic status and the extent of motor impairment among the children ($p=0.419$) (Table 1).

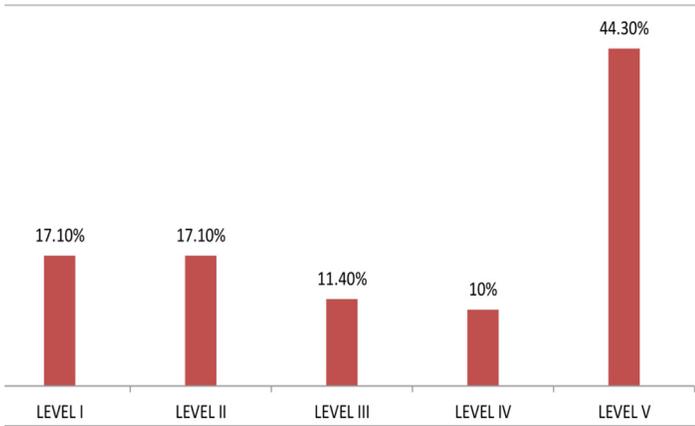


Figure 2: Gross motor function classification of subjects

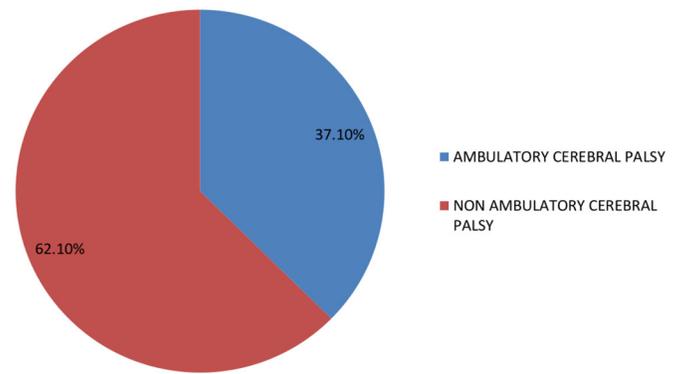


Figure 3: Subclassification of cerebral palsy into ambulatory and non-ambulatory

Table 1: Relationship between GMFCS and Socio-economic class (SEC)

	Ambulatory	Non-ambulatory	Total	X ² Value	p-value
Upper SES	7 (26.9%)	15(34.1%)	22 (31.4%)	1.738	0.419
Middle SES	6(23.1%)	14(31.8%)	20(28.6%)		
Lower SES	13(50%)	15(34.1%)	28(40%)		
Total	26	44	70		

Relationship between GMFCS and risk factors for CP

Perinatal asphyxia was the most frequently encountered risk factor for developing CP, as documented in 48.6% of the subjects. Neonatal jaundice, CNS infection and the existence of multiple risk factors were all observed to have a significant relationship with the degree of motor impairment (p=0.038, p=0.019, p=0.028 respectively). The odds of having ambulatory CP is increased when CNS

infection is an identifiable risk (p value=0.019, CI=1.198-9.650, OR=3.400). This is also the case among children with only one identifiable risk for developing CP (p=0.028, CI=1.113-10.702, OR=3.451). In the same vein, the odds of having non-ambulatory CP are higher among those with neonatal jaundice as a risk factor (p value=0.038, CI=1.118-0.961, OR=0.336). However, nine children had no identifiable risks for the development of CP (Table2).

Table 2: Relationship between GMFCS and risk factors for CP

		Ambulatory	Non-ambulatory	Total	X ² Value	p-value	Odds ratio C I	Value
Asphyxia	Yes	10(38.5%)	24(54.5%)	34(48.6%)	1.692	0.193	0 . 1 9 4 - 1.399	0.521
	No	16(61.5%)	20(45.5%)	36(51.4%)				
	Total	26	44	70				
Prematurity	Yes	1(3.80%)	7(15.9%)	8 (11.4%)	2.349	0.125 [#]	0 . 0 2 4 - 1.826	0.211
	No	25(96.2%)	37(84.1%)	62(88.6%)				
	Total	26	44	70				
Neonatal jaundice	Yes	7(26.9%)	23(52.3%)	30(42.8%)	4.280	0.038 [*]	0 . 1 1 8 - 0.961	0.336
	No	19(73.1%)	21(47.7%)	40(57.1%)				
	Total	26	44	70				
CNS infection	Yes	13(50%)	10(22.7%)	23(32.9%)	5.510	0.019 [*]	1 . 1 9 8 - 9.650	3.400
	No	13(50%)	34(77.3%)	47(67.1%)				
	Total	26	44	70				
Number of risk factors	Single	16(72.7%)	17(43.6%)	33(54.1%)	4.809	0.028 [*]	1 . 1 1 3 - 10.702	3.451
	Multiple	6(27.3%)	22(56.4%)	28(45.9%)				
	Total	22	39	61 ^{&}				

[#]Fisher's exact, ^{*}Significant, [&]Nine subjects had no identifiable risk factors

Relationship between GMFCS and CP related comorbidities

Speech impairment was documented in 48.6% of the subjects and was the most prevalent comorbidity. This was closely followed by seizure disorder, as demonstrated in 47.1% of the children. In addition, the occurrence of two or more CP-associated comorbidities was found in 21.7% of the children. While most of the children with comorbidities were observed to have non-ambulatory forms of motor impairment, there was no significant relationship between the presence of any particular comorbidity and the degree of motor impairment. There were no identifiable co-morbidities in ten children (Table 3).

in 44% of the children, while level III was the least observed. We also noted that the majority of the subjects had the spastic form of CP and most of the children were non-ambulatory. Furthermore, our study found no significant relationship between motor impairment and the parents' socio-economic status, nor was there any significant association between CP-related comorbidities and the degree of gross motor impairment. However, the children that had only one identifiable risk for developing CP, as well as those with hemiplegic CP, had higher odds of being ambulatory. In addition, children with neonatal jaundice as an identifiable risk, those with multiple risk factors, and

Table 3: Relationship between GMFCS and CP related comorbidities

		Ambulatory	Non-ambulatory	Total	X ² Value	p-value
Visual impairment	Yes	5 (19.2%)	14(31.8%)	19(27.1%)	1.309	0.253
	No	21(80.8%)	30(68.2%)	51(72.9%)		
	Total	26	44	70		
Speech impairment	Yes	12(46.2%)	22(50%)	34(48.6%)	0.097	0.756
	No	14(53.8%)	22(50%)	36(51.4%)		
	Total	26	44	70		
Seizure	Yes	13(50%)	20(45.5%)	33(47.1%)	0.136	0.713
	No	13(50%)	24(54.5%)	37(52.9%)		
	Total	26	44	70		
Impairment in adaptive behavior	Yes	5(19.2%)	8(18.2%)	13(18.6%)	0.012	0.900
	No	21(80.8%)	36(81.8%)	47(81.4%)		
	Total	26	44	70		
Muscle contractions	Yes	4(15.4%)	9(20.5%)	13(18.6%)	0.278	0.598
	No	22(84.6%)	35(79.5%)	57(81.4%)		
	Total	26	44	70		
Number of co-morbidities,	Multiple	5(22.7%)	8(21.1%)	13(21.7%)	0.023	0.879
	Single	17(77.2%)	30(78.9%)	47(78.3%)		
	Total	22	38	60*		

*Ten subjects had no identifiable co-morbidities

Relationship between GMFCS and forms of CP

Most children had spastic CP (83%), while extrapyramidal CP (choreoathetoid especially) was seen in only 5.7%. Quadriplegic CP accounted for 42.9%, Hemiplegic CP was found in 17.1%, 22.9% had diplegia and 4.3% had the mixed form. The clinical form of CP could not be ascertained in five subjects. The majority (91.7%) of those that had hemiplegic CP were ambulatory ($p=0.000$, $CI=3.748-265.300$, $OR=31.533$), while almost all the subjects with spastic quadriplegia were non-ambulatory ($p=0.000$, $CI=0.010-0.228$, $OR=0.048$) (Table 4).

DISCUSSION

This study has profiled the gross motor function of children with CP at ATBUTH Bauchi, Nigeria. The prevailing risk factors, the forms of CP, as well as CP-related co-morbidities, were identified and their relationship with motor impairment, was established. We found GMFCS level V to be the most common, as this was demonstrated

those with quadriplegic CP were more likely to have non-ambulatory CP.

The occurrence of severe motor impairment in the majority of the subjects we studied is similar to what has been previously observed in other parts of Nigeria and other developing countries. Adekoje et al. [14], in Lagos, reported that 40% of the CP cases were at GMFCS level V and about 65% were non-ambulatory. Similarly, Esegbe et al. in Zaria [15] found severe motor impairment among 60.9% of children with CP. In Botswana, Bearden et al. [10] reported non-ambulatory CP in 57% of the children studied. These observations contrast sharply with the results in many high-income countries (HICs). In two separate population-based studies in Victoria, Australia [16] and Quebec Canada [17], it was reported that 68% and 66% respectively of children with CP were ambulatory. This disparity may be explained by better access to rehabilitative care in HICs. Furthermore, many of the studies conducted in sub-Saharan Africa have consistently revealed perinatal asphyxia as the

Table 4: Relationship between GMFCS and CP related comorbidities

		Ambulatory	Non-ambulatory	Total	X ² Value	p-value	Odds ratio CI	Value
Hemiplegic	Yes	11(42.3%)	1(2.3%)	12(17.1%)	18.4	<0.0001*	3.748 - 265.300	31.533
	No	15(57.7%)	43(97.7%)	58(82.9%)				
	Total	26	44	70				
Diplegic	Yes	7(26.9%)	9(20.5%)	16(22.9%)	0.388	0.533	0.461 - 4.456	1.433
	No	19(73.1%)	35(79.5%)	54(77.1%)				
	Total	26	44	70				
Quadriplegic	Yes	2(7.7%)	28(63.3%)	30(42.9%)	20.886	<0.0001*	0.010 - 0.228	0.048
	No	24(92.3%)	16(36.4%)	40(57.1%)				
	Total	26	44	70				
Dyskinetic	Yes	1(3.8%)	3(6.8%)	4(5.7%)	0.268	1.000 [#]	0.054 - 5.547	0.547
	No	25(96.2%)	41(93.2%)	66(94.3%)				
	Total	26	44	70				
Mixed	Yes	0(0%)	3(6.8%)	3(4.3%)	1.852	0.289 [#]	1.350 - 1.977	1.634
	No	26(100%)	41(93.2%)	67(95.7%)				
	Total	26	44	70 ^{&}				

[#] Fisher's exact, *Significant, [&] Five subjects did not fit into any of the above classifications of CP

single most important risk for developing CP. While some studies have reported a similar pattern in HICs, unlike in most developing economies, the widespread availability of interventions such as head cooling in HICs has been shown to significantly reduce the occurrence and the severity of permanent neurological sequelae [18,19]. Thus, the difference in the approach to the management of adverse intrapartum and neonatal events may be a possible explanation for the greater occurrence of non-ambulatory CP in many developing countries.

The odds of being non-ambulatory was increased by greater than three folds among children with CP, who had two or more risk factors. This is in contrast to the study by Iloeje et al. in Enugu [9], who reported no significant association between the multiplicity of risks for developing CP and the degree of the subsequent motor impairment. The coexistence of perinatal asphyxia, CNS infection and jaundice was particularly common in our study, and it seems plausible that this could have resulted in more extensive brain damage among the affected children, thus resulting in severe motor impairment. Moreover, another study has previously suggested the additive effect of multiple risk factors on CP outcome [20]. We also found jaundice to be a common risk for developing CP, as it was only second to perinatal asphyxia. Indeed, the occurrence of jaundice increased the odds of developing severe motor impairment. Such is not the case in HICs, where jaundice has been reported as a less common cause of CP [17]. This may be evidence of inadequate resources and manpower required to promptly identify and properly treat jaundice among the new-born in our environment.

Unlike some previous studies, we did not observe a significant association between the presence of co-morbidities and the severity of motor impairment [9,10]. This is despite the presence of comorbidities in 86% of the participants. Although most of those with comorbidities in our study were non-ambulatory, our comparatively

smaller sample size may explain why the observations were not statistically significant.

Like previous reports, we did not find any correlation between the parents' socio-economic background and the GMFCS [9]. This probably reflects the non-discriminative exposure to similar risk factors for CP across different social classes.

Spastic CP was the most prevalent physiological form, accounting for 82.9% of cases. This is similar to what has been reported in other studies in sub-Saharan Africa. Quadriplegic CP was the major topographic pattern observed, similar to previous studies [9,10]. This is also the case in many reports from HICs, despite disparities in the pattern of aetiologies of CP between HICs and developing countries [8,16-18]. Furthermore, we found higher odds of having ambulatory CP among children with spastic hemiplegia and non-ambulatory CP in most quadriplegic cases. This agrees with findings in the literature [8-10]. The establishment of such a link between the clinical subtype of CP and ambulatory potential is vital, as this may have an important implication on parents' counseling about future motor outcomes.

Despite highlighting the variables that may influence the ambulatory outcome of children with CP, the limited sample size and the possible confounding effects of some of the identified risks for developing CP, are the major limitations to this study.

CONCLUSION

Our study has further reaffirmed that the majority of children with CP in developing countries are non-ambulatory. We have also demonstrated that the presence of multiple risk factors significantly decreases ambulatory potential. Harnessing efforts targeted at preventing the occurrence of adverse events such as asphyxia and neonatal jaundice may limit the severity and bur-

den of CP in developing countries. Furthermore, we found that the clinical form of CP has significant links with ambulatory outcomes. Thus, proper identification of the clinical subtype of CP is imperative, as this may influence counseling on motor potentials and future management trajectory.

REFERENCES

- [1] P. Rosenbaum, N. Paneth, A. Leviton, M. Goldstein, and M. Bax, "The definition and classification of cerebral palsy," *Dev Med Child Neurol*, vol. 49, pp. 1–44, Jan. 2007.
- [2] G. E. Ofovwe and M. O. Ibadan, "Pattern Of Neurological Disorders In Child Neurology Clinic Of The University Of Benin Teaching Hospital, Benin City, Nigeria," *Annals of Biomedical Sciences*, vol. 6, no. 1, pp. 18-27–27, Jan. 2007.
- [3] R. D. Wammanda, R. Onalo, and S. J. Adama, "Pattern of neurological disorder presenting at a pediatric neurology clinic in Nigeria," *Ann Afr Med*, vol. 6, no. 2, pp. 73–75, Jun. 2007.
- [4] I. N. Mohamed, M. A. Elseed, and A. A. Hamed, "Clinical Profile of Pediatric Neurological Disorders: Outpatient Department, Khartoum, Sudan," *Child Neurol Open*, vol. 3, doi:2329048X15623548, Dec. 2016.
- [5] K. I. Eyong, A. A. Asindi, and C. Terty, "Aetiology and comorbidities of cerebral palsy in a developing country," *International Journal of Research in Medical Sciences*, vol. 6, no. 10, pp. 3246–3250, Sep. 2018.
- [6] R. O. Belonwu, G. D. Gwarzo, and S. I. Adeleke, "Cerebral palsy in Kano, Nigeria--a review," *Niger J Med*, vol. 18, no. 2, pp. 186–189, Jun. 2009.
- [7] R. Palisano, P. Rosenbaum, S. Walter, D. Russell, E. Wood, and B. Galuppi, "Development and reliability of a system to classify gross motor function in children with cerebral palsy," *Dev Med Child Neurol*, vol. 39, no. 4, pp. 214–223, Apr. 1997.
- [8] M. I. Shevell, L. Dagenais, N. Hall, and REPACQ CONSORTIUM*, "The relationship of cerebral palsy subtype and functional motor impairment: a population-based study," *Dev Med Child Neurol*, vol. 51, no. 11, pp. 872–877, Nov. 2009.
- [9] S. O. Iloeje and C. C. Ogoke, "Factors associated with the severity of motor impairment in children with cerebral palsy seen in Enugu, Nigeria," *South African Journal of Child Health*, vol. 11, no. 3, pp. 112-116–116, Jan. 2017.
- [10] D. R. Bearden et al., "Pediatric Cerebral Palsy in Botswana: Etiology, Outcomes, and Comorbidities," *Pediatric Neurology*, vol. 59, pp. 23–29, Jun. 2016.
- [11] O. Olusanya, E.E. Okpere, and M. Ezimokhai, "The importance of social class in voluntary fertility control in a developing country". *West African Journal of Medicine*, 4, 205-207, 1985
- [12] American Speech-Language-Hearing Association (2020, July 1st) *Child speech and language* (online). Available: <https://www.asha.org/public/speech/disorders/ChildSandL/>
- [12] American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Washington, DC, American Psychiatric Association 2000.
- [13] TO Adekoje, MN Ibeabuchi, FE Lesi. "Anthropometry of children with cerebral palsy at the Lagos University Teaching Hospital". *J Clin Sci*, vol.13, pp. 96-104, Jul. 2016.
- [14] EE Esegbe et al. "A Review of Gross Motor Function in Children with Cerebral Palsy in Zaria, North-Western Nigeria". *Int J Phys Med Rehabil*, vol 2, pp.236, Sept. 2014
- [15] S. M. Reid, J. McCutcheon, D. S. Reddihough, and H. Johnson, "Prevalence and predictors of drooling in 7- to 14-year-old children with cerebral palsy: a population study," *Dev Med Child Neurol*, vol. 54, no. 11, pp. 1032–1036, Nov. 2012.
- [16] M. I. Shevell, L. Dagenais, N. Hall, and REPACQ Consortium, "Comorbidities in cerebral palsy and their relationship to neurologic subtype and GMFCS level," *Neurology*, vol. 72, no. 24, pp. 2090–2096, Jun. 2009.
- [17] S. McIntyre, D. Taitz, J. Keogh, S. Goldsmith, N. Badawi, and E. Blair, "A systematic review of risk factors for cerebral palsy in children born at term in developed countries," *Dev Med Child Neurol*, vol. 55, no. 6, pp. 499–508, Jun. 2013.
- [18] A. D. Edwards et al., "Neurological outcomes at 18 months of age after moderate hypothermia for perinatal hypoxic-ischaemic encephalopathy: synthesis and meta-analysis of trial data," *BMJ*, vol. 340, p. c363, Feb. 2010.
- [19] K. B. Nelson and T. Chang, "Is cerebral palsy preventable?," *Curr. Opin. Neurol.*, vol. 21, no. 2, pp. 129–135, Apr. 2008.