Published in final edited form as:

AIDS Care. 2018 May ; 30(5): 618–622. doi:10.1080/09540121.2018.1426829.

Neurocognitive functioning of HIV positive children attending the Comprehensive Care Clinic at Kenyatta National Hospital: Exploring neurocognitive deficits and psychosocial risk factors.

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Introduction

In Kenya, the prevalence of new HIV infection among adolescents has increased from 29% in 2014 to 49% in 2016 (NACC, 2016). Despite having access to ARVs, neurocognitive deficits are a burgeoning issue in HIV infected children (Boyede, Lesi, Ezeaka & Umeh, 2013). Studies have conflicting evidence with their cognitive development being in normal range (Bagenda et al. 2006; Brahmhatt et al. 2014; Ravindran, Rani & Priya 2014) to others pointing to considerable cognitive deficits (Koekkoek et al. 2008; Boyede et al. 2013). Additionally, it has been found that adverse psychosocial factors further deteriorate cognitive functioning of children and adolescents living with HIV (CALWH) (Busman, Page, Oka, Giordiani and Boivin, 2013).

Our objective was to assess the neurocognitive functioning of CALWH using Kaufman Assessment Battery for Children (second edition) and correlate how these findings map on to psychosocial domains tapped via HEADS-ED.

Recent studies from Uganda (Boivin et al., 2016, Boivin et al., 2010, Ruel et al, 2012), South Africa (Laughton et al., 2009) and Nigeria (Boyede et al., 2013a, Boyede et al., 2013b, Boyede et al., 2013c) have noted significant neurocognitive deficits. Thus identifying these deficits earlier would enable timely neurocognitive rehabilitation with development of psychosocial and educational interventions.

Methods

Setting

The study was conducted at Kenyatta National Hospital (KNH), Comprehensive Care Centre (CCC) and received Institutional Research Board (approval no. P265/03/2016) from KNH/ University of Nairobi). The first author was trained by PB and MK in administering the KABC-II.

Study Population

We recruited 90 CALWH of ages 8–15 years who are on HAART using purposive sampling. CALWH but not on HAART, who have neurological disease such as meningitis, and attending special school or with physical disabilities were excluded.

Material and Measures

Sociodemographic questionnaire

Caregivers provided information on their relationship with children, their education and home information and health status.

Kaufman Assessment Battery for Children, Second Edition

KABC-II has been adapted and validated in Kenya and Uganda in diverse populations (Bagenda et al., 2004; Bangirana et al., 2009). We have used the Luria model that is embedded within the KABC conceptual and scoring framework. Thirteen subtests were used to generate four index scores (sequential, simultaneous, planning, and learning) and the global score called Mental Processing Index (MPI). We did not administer the knowledge subtests due to limited cultural suitability (Boivin et al., 2010).

HEADS-ED tool

HEADS-ED is a mnemonic for Home, Education, Activities and peers, Drugs and alcohol, Suicidality, Emotions, behavior and thought disturbance and Discharge resources (Capelli et al., 2012). It acts as an indicator of psychosocial risks and protective factors impacting children's lives; entailing a simple scoring system with seven variables rated on three-based scale of need of action as evaluated by Capelli et al. (2012) in Canada. This showed the sensitivity of 82% and specificity of 87% in predicting pediatrics patients with mental health. The use of this tool by postgraduate pediatric studies at University of Nairobi, motivated us to test its use in the HIV clinic. It is a rapid screener complementing neurocognitive assessment battery.

Data Collection Procedure

Eligible participants were recruited until the desired sample was obtained. Written assent and informed consents from guardians and young participants were sought and then a sociodemographic coupled with caregiver questionnaires were administered. KABC-II and HEADS-ED screening tools were administered on each participant in a well-lit comfortable room. Participants were given breaks to minimize fatigue and served light refreshments.

Data Analysis

SPSS v23 (reference) was used to generate descriptive statistics including means (*SD*) and percentages which were calculated for sociodemographic characteristics of participating children and caregivers. Independent sample t-test was used to establish the differences between KABC standardize to determine how dichotomized variables like immune function (<200 CD4 count and >200 CD4 count), viral load (<1000copies ml or >1000copies ml) and ARV initiation (<30months or >30months) mapped on MPI score. A composite index of HEADS-ED used as an independent variable was computed by calculating a summative score (ranging from 0 to 6) using responses from individual domain items. Linear regression were used to assess KABC scores correlations with CD4 count, viral load, HEADS-ED. A *p* value 0.05 was considered statistically significant. Multivariate linear regression analysis was used to determine child and caregiver characteristics effects with respect to school performance and their interaction with MPI score.

Results

Demographic Characteristics of the Respondents and Caregivers

Of the 90 participants, 54.4% (*n*=49) were boys and 45.6% (*n*=41) girls. The mean age was 11.38 (*SD* ± 2.06) years and 26.7% were 11 years old (see Table 1).

Neurocognitive and treatment outcomes

The prevalence of major neurocognitive disorder (MND) using MPI score suggests that 60% (*n*= 54) participants were at least 2 *SD* below the mean. High prevalence of MND was seen in simultaneous processing (62.2%), planning (63.3%) and NVI (74.4%) subscales. Only 4/90 (4.4%) were found with significant immunosuppression based on current WHO guidelines.

Most participants –76.7% (*N*= 69) had low viral loads (< 1000 copies per ml) implying good adherence and viral suppression. No significant associations between MPI (*p*=0.06), sequential (*p* = 0.09), planning (*p* = 0.22), learning (*p* = 0.06) and simultaneous (*p* = 0.26) in KABC II performance of participants with high vs low VLs were found. Twenty-eight (31.5%) participants were enrolled into care and initiated into ARVs within 30 months of diagnosis.

HEAD-ED assessment of risk and protective factors and its association with neurocognitive performance

The six items in the HEADS-ED tool were used to evaluate if KABC-II scores are related to psychosocial risk factors and protective factors against MND. Problems were found on domains of education (41.1%), activities and peers (20%) and emotionality & behavior-thought disturbance (20%) with 40 (44.4%) participants not reporting any significant problems.

HEADS-ED risk factors and poor neurocognitive performance using the global MPI score was not statistically significant but noteworthy ($\beta = -1.87$, $p=0.06$). Analyses at sub-domain level revealed that education ($\beta = -5.67$, $p=0.02$) and activities and peer support ($\beta = -9.1$, $p=0.002$) were significantly associated with poor neurocognitive performance, with participants experiencing education domain problems scored 5.67 points lower than those not reporting problems and those with problems related to activities and peers scored 9.1 points lower respectively.

Multivariate regression analysis

Findings of multivariate analysis (see table 2) demonstrate an R^2 of 0.44, implying that independent variables in the model explain 44% of the total variation seen in neurocognitive performance.

Discussion

From our overall sample, 54 participants (60%) lie 2SD below the mean (indicating presence of a major neurocognitive disorder) using MPI score. This is comparable to other studies that found 56.5% of the HIV positive children aged 6–15 had below average cognitive functioning and similar impairments were observed in perinatally infected children on HAART (Boyede et al., 2013; Ruel et al., 2012; van Loon 2009; Koekkoek et al., 2008).

Findings on relationship between neurocognitive outcomes, immune status and viral loads have differed with regards to outcomes. Ruel et al. (2012) demonstrated significant motor and cognitive deficits among CLWH with CD4 count of ≤ 350 and those with High VLs ($>50,000$ copies/ml) had poor neurocognitive functioning (Jeremy et al 2005). However, van Loon (2009) found poorer neurocognitive performance in CLWH than HIV negative children regardless of the stage of disease, immune status, or ART regimen.

Our findings demonstrate that early or late initiation in ARVs within 30 months after birth was not associated with improved KABC performance. Puthanakit et al. (2012) found the same in Thai and Cambodian children. However, Crowell et al. (2015) showed that early treatment results in improved cognitive outcome. Given the rich scholarship on complex causal pathways of deficits, we believe that cognitive deficits in CLWH may potentially occur in infancy and may not improve necessarily with early initiation of ART. Psychosocial adjustment problems in CALWH have been discussed in literature (Zalwango et al., 2016). Our analyses of HEADS-ED reveals that our participants were experiencing considerable problems at school; also the greater the dissatisfaction a caregiver expressed about school performance, the lower the scores on MPI. These results are consistent with Brahmabhatt et

al. (2017) who found that continuation of studies yields a reduction of cognitive deficits by 30%–40% among CALWH.

Due to the cross-sectional nature of the study, we cannot make any causal associations. The study was based in one urban public hospital, it is difficult to generalize it to a wider population. The sample size was sufficient for a pilot initiative however a larger one would provide statistical power leading to more robust conclusions. There was no comparison group so our sample was homogenous resulting in equitable distribution of risks. Further, HEADS-ED can be used to screen not evaluate psychosocial problems in-depth.

Conclusion

We detected that sixty percent of our sample had major neurocognitive deficits with scores below 2SD. This outcome was not influenced by viral load or CD4 count, medication or early initiation in HIV cascade of care. Neurocognitive functioning was related to school performance and reduced by 5.7 points when participants experienced problems in educational domain assessed via HEADS-ED tool.

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Table 1:

Demographic Characteristics of the Respondents and Caregivers

Variable	Category	Frequency (N=90)	Percent (%)
Age in years	(Mean, SD, Range)	(11.38, 2.06, 8–15)	
Age in years	10-Aug	20	22.2
	15-Nov	70	77.8
Gender	Male	49	54.4
	Female	41	45.6
	Below 30 months	28	31.5
Age enrolled in HIV (n = 89)	Above 30 months	61	68.5
	Stage 1	75	88.2
WHO Clinical Stage (n = 85)	Stage 2 or 3	10	11.8
	Above 200	4	4.4
Current CD4 Count	Below 200	86	95.6
	Below 1000	69	76.7
Viral load copies ml	Above 1000	21	23.3
	First line	66	78.9
Medication	Second line	19	21.1
Caregiver sociodemographic			
Gender	Male	14	15.6
	Female	76	84.4
	Below 20	7	7.8
	21–35	27	30
	36–50	47	52.2
Age	Above 50	8	8.9
	Father	8	8.9
	Mother	57	63.3
	Relative/friend	20	22.2
Relationship to the child	Other (Children's home)	5	5.6
	Single	32	35.6
	Married	39	43.3
	Widowed	14	15.6
Marital Status	Separated	5	5.6
	University/college	17	18.9
	Secondary	28	31.1
Educational level	Primary/none	45	50
	Yes	57	63.3
Employment	No	31	34.4
	< KShs 3999	19	26.4
	KShs 4000–5999	17	23.6
Monthly Income	KShs 6000–9999	10	11.1

Variable	Category	Frequency (N=90)	Percent (%)
Disclosure	Above KShs 10000	26	28.9
	Yes	61	67.8
	No	29	32.2
	Very satisfied	11	12.2
Child performance	Satisfied	30	33.3
	Neutral	28	31.1
	Unsatisfied	15	16.7
	Very unsatisfied	4	4.4
Repeated grade	Yes	36	40
	No	53	58.9
Child's attendance	Often misses school	11	12.2
	Occasionally misses school	16	17.8
	Rarely misses school	61	67.8
	Not going to school	2	2.2
	Financial problems	8	27.6
	Due to illness	14	48.3
Reason for missing School (n = 29)	Other	7	24.1

Table 2:

Multivariate regression analysis of child factors and caregivers characteristics, school performance and MPI

	β coefficient	Std. Err.	P	95% CI	
HEADS-ED					
Education	-1.27	2.59	0.63	-6.46	3.91
Activities and Peers	-5.30	2.95	0.08	-11.20	0.60
Viral load (> 1000 per ml)	4.28	3.09	0.17	-1.89	10.46
School performance					
Satisfied	-5.28	3.83	0.17	-12.94	2.38
Neutral	-8.57	4.00	0.04	-16.56	-0.58
Unsatisfied	-9.39	4.41	0.04	-18.20	-0.57
Very unsatisfied	-15.20	6.40	0.02	-28.00	-2.41
Never repeated school grade	4.14	2.38	0.09	-0.62	8.90
Relation with child					
Mother	-2.77	6.20	0.66	-15.16	9.62
Relatives	0.22	5.67	0.97	-11.13	11.56
Other	-0.07	8.16	0.99	-16.39	16.25
Male caregiver	-5.35	5.01	0.29	-15.37	4.66
Child's age	0.05	0.65	0.94	-1.24	1.34
Enrolled in care > 30 month	3.37	2.72	0.22	-2.06	8.80
WHO HIV clinical stage					
2	-4.67	4.69	0.32	-14.04	4.70
3	4.84	5.32	0.37	-5.79	15.47
Current CD4 count	0.00	0.00	0.99	-0.01	0.01
Constant (Intercept)	68.87	11.94	0.00	45.00	92.75