# Childhood Autism Spectrum Disorder:
## *Insights From A Tertiary Hospital Cohort In Kenya*

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## Summary

**INTRODUCTION**

**Autism Spectrum Disorder (ASD) is characterized by impairments in behavior, social communication and interaction. There have been little data on ASD from sub-Saharan Africa (SSA) describing clinical characteristics in large cohorts of patients. Preliminary studies reported a high male sex ratio, excess of non-verbal cases, possible infectious etiologies and comorbidities e.g. epilepsy.**

**OBJECTIVES**

**To describe the clinical characteristics of children diagnosed with ASD in an African context.**

**METHODOLOGY**

**This cohort study used a retrospective medical chart review which identified 116 (7%) children diagnosed with ASD according to DSM-5 criteria. From a total of 1,711 medical records consisting of physical files and electronic databases from Twenty-seven (23%) children self-referred while 89 (77%) referred by other medical practitioners and attended a pediatric neurology clinic at Aga Khan University Hospital in Nairobi, Kenya, between 2011 and 2016.**

**RESULTS**

**The median age at presentation was 3 years with speech delay as the most common reason for presentation enventhouh most of them were 6 years and below. Expressive language delay was observed in 90% of the respondents. (60%) who obtained imaging had normal MRI brain findings. Only 44% and 34% of the children had access to speech and occupational therapy respectively. 53% in the study were first-borns in their families. Epilepsy and ADHD were the most prevalent co-morbidities. Males (94, 81.1%) were more than females (22, 18.9%) at a ratio of 4.3:1.**

**CONCLUSION AND RECOMMENDATIONS**

**An early median age at presentation and preponderance of male gender was observed as lack of awareness and stigma identified as contributing factors for therapy. Access to speech therapy and other interventions to scale-up to cub intellectual disability and epilepsy. A prospective study would help determine outcomes following appropriate interventions from 1 to 23 years old.**

***Keywords:*** **Autism,Sub-Saharan Africa, Comorbidities, Language delay,Intellectual disability, Birth history**

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## Introduction

Autism spectrum disorder (ASD) is a neuro-developmental disorder characterized by impairments in social communication and interaction, restricted or repetitive patterns of behavior, interests, and activities. The burden of ASD in Sub-Saharan Africa (SSA) remains unclear owing to the lack of large scale population studies in this region [1].

A high prevalence was observed in males, with intellectual disability and epilepsy reported as the most common co-morbidities, high proportion of non-verbal cases of ASD, and possible infectious disease *etiology* have been described in SSA. Under-diagnosis and late presentation were common where a median age of 8 years at presentation was reported in some areas. That indicated excesses of non-verbal cases of ASD (71%), compared to 25% in developed countries.

Studies in Tanzania and Kenya describe a close temporal relationship between severe malaria and the diagnosis of ASD. [6, 11]

Magnetic Resonance Imagining (MRI) ab-normalities have been documented in children with ASD in high resource countries but there was no data from SSA. White Matter *Hyper-intensities* (WMH) in regions of brains of children with ASD was reported, associated with cognitive and functional impairments which could be of particular relevance to behavioral impairment observed in ASD [12 - 14].

Furthermore, previous research had shown an increase of cerebral *hyper-intensities* among patients diagnosed with neuropsychiatric disorders such as Attention Deficit Hyperactivity Disorder (ADHD). A common co-morbidity among ASD patients. [15]

## Material and Methodology

## Objectives

The aim of this study was to describe specific characteristics of children diagnosed with ASD based on data from Aga Khan University Hospital in Nairobi, Kenya. This hospital is an urban, private not for profit institution, which provides emergency and follow-up services for the resident population and also functions as a referral hospital within the Eastern African region.

## Study Design

This was a retrospective cross-sectional study of patient medical records that identified children with a diagnosis of ASD between 2011 and 2016. Patient medical records consisted of physical files and electronic databases.

## Participants

There were parents of children with concerns for behavioral and neurodevelopment disorders who were either self-referred by their families or by their pediatrician.

## Procedure

Clinical observation following comprehensive interviews with parent and child by two experienced pediatric neurologists evaluated all respondents and utilized the same criteria to make the diagnosis of ASD.

Children who met the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition were diagnosed to have ASD. Both neurologists assessed respondents for co-morbidities such as Attention Deficit Hyperactivity Disorder (ADHD) and epilepsy using standard screening tests and clinical evaluation. A diagnosis of ADHD was made in patients who fulfilled the DSM 5 criteria. A Criteria established by the International League against Epilepsy (ILAE) diagnosis [16].

A research assistant extracted data from the relevant medical charts according to pre-determined criteria. Each medical record was allocated a unique study identification number at the time of data entry to maintain patient confidentiality. Ethical Approval was sought and obtained from the Human Ethics Research Committee at Aga Khan University Hospital prior to the beginning of the study.

Variables of interest were obtained, coded and entered into a Microsoft Excel spreadsheet. These variables include:

- Presenting complaints
- Anthropometric measures
- Birth
- Developmental and family history
- Co-morbidities
- Features of learning disability (if present)
- Referral status.

## Measures

Anthropometric data was documented using growth charts developed by the Centers for Disease Control (CDC). [17]

The Modified Checklist for Autism in Toddlers, Revised (M-CHAT-R) version was administered to parents of children between 16 and 30 months of age. The M-CHAT- R had been validated in international settings and demonstrated adequate psychometric properties to effectively assess risk for developing ASD among children 16 – 30 months of age. The M-CHAT-R consists of 20 questions coded with pass or fail criteria according to the following scoring algorithm. Those who failed 3 – 7 items were classified as having a medium risk of an eventual diagnosis of ASD while those who failed more than 7 items were classified as at high risk for ASD. [18, 19]

In the context of high burden of CNS infections and other environmental causes of neurological challenges with developmental disabilities in SSA, MRI brain scans were done to establish neuroimaging evidence for such factors as contributory in individual cases. Radiology reports from those MRI brain scans, as available in the clinical records, were reviewed. All MRI reports were anonymized prior to the collection and analysis of subject data. Clinical findings recorded in reports was summarized and classified as:

- Normal findings,
- White matter abnormalities,
- Gray matter abnormalities,
- Congenital malformations,
- Local infarcts,
- Heterogeneous lesions.

## Data Analysis

Statistical analysis was conducted using IBM statistics SPSS version 23 software. Data were summarized using descriptive statistics, including frequencies, proportions, means, standard deviations, and median as appropriate. For variables with missing data, the analysis was confined to available data.

# RESULTS

## Demographics

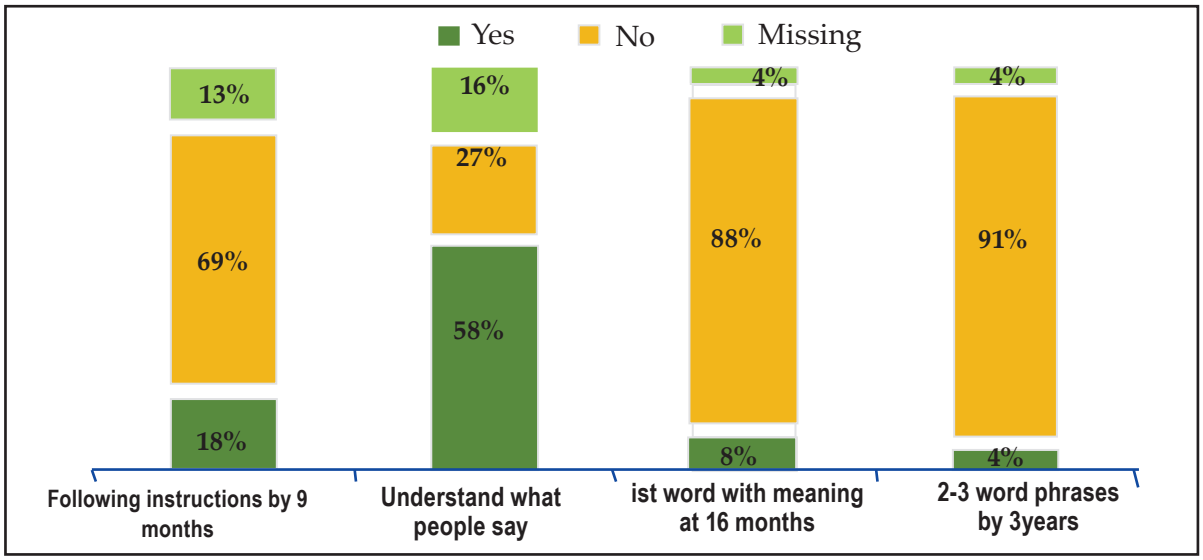
A total of 1,711 medical records were identified from children who attended the neurology clinic during the study period. 116 (7%) were records of children with a diagnosis of ASD. The baseline characteristics of the study population is presented in ***Table 1.***

Among the children with ASD, the median age at presentation was 3 years with the age range being 1 to 23 years. There were more males (94, 81.1%) than females (22, 18.9%) at a ratio of 4.3:1. Twenty-seven (23%) children in this cohort were self-referred while 89 (77%) were referred by other medical practitioners.

## Presenting Complaints

Delayed language development was the most common reason for presentation to the pediatric neurology clinic and was reported in 102 (87.9%) children, as they had not spoken their first word by 16 months. Only $n$ = 21 (18.1%) could follow simple instructions by 9 months of age (***see Figure 1)***.

***Figure 1:*** *Bar Graph Illustrating Language Development in Children with Autism*



Auditory assessments were conducted for 43 (37.1%) children of whom 5 (4.3%) were reported to have impaired hearing. The uptake of speech therapy and occupational therapy was documented for 51 (43.9%) and 40 (34.4%) children respectively following evaluation. In a range of 8-36 months, the median age for the first step of walking regardless was 12 months. Hyperactivity as a presenting complaint was reported as a significant concern in 59 (50.9%) children while a short attention span was documented for *n*=25 (21.6%) children (***See Table 1).***

***Table 1:*** *Demographic Characteristics and Summary of Presenting Complaints.*

| **Age (years)** | ***n*** **= 116** | **%** | |
|---|---|---|---|
| 1-3 | 62 | 53.4 | |
| 4-6 | 33 | 28.5 | |
| 7-9 | 11 | 9.5 | |
| 10-12 | 7 | 6.0 | |
| 13-23 | 3 | 2.6 | |
| **Gender** | | | |
| Male | 94 | 81 | |
| Female | 22 | 19 | |
| **Residence** | | | |
| Urban | 110 | 94.8 | |
| Rural | 6 | 5.2 | |
| **Chief complaint** | **N** | **%** | **CI** |
| Speech delay | 110 | 94.8 | (90.8% -98.8%) |
| Hyperactivity | 59 | 50.9 | (41.8%-60%) |
| Short attention span | 25 | 21.6 | (14.1%-29.1%) |
| Aggressive behaviour | 19 | 16.4 | (9.7%-23.1%) |
| Poor motor function | 10 | 8.6 | (3.5% - 13.7%) |
| Learning difficulties | 9 | 7.8 | (2.9%-12.7%) |
| Jerky movements | 7 | 6 | (1.7%- 10.3%) |
| Staring episodes | 6 | 5.2 | (1.2% -9.2%) |

***Note:*** *Some patients had more than one complaint recorded.*

## Birth Circumstances

Pre-term births occurred in 10 (8.6%) children while vaginal delivery was reported for 51 (44%). Caesarian section delivery was recorded for *n*=45 (38.8%) children. Neonatal sepsis and meningitis were reported for 10 (8.6%) and 5 (4.3%) patients respectively. More details regarding the cohort birth details are provided in ***Table 2.***

***Table 2 :*** *Maternal Factors and Birth History*

| **Variables (n=116)** | N | % |
|---|---|---|
| Birth history | | |
| Term births | 84 | 72.4 |
| Preterm births | 10 | 8.6 |
| Missing data | 22 | 19 |
| **Mode of delivery** | | |
| Vaginal delivery | 51 | 43.9 |
| CS due to slow progression of labor | 15 | 12.9 |
| CS due to fetal distress | 9 | 7.8 |
| CS due to previous scar | 9 | 7.8 |
| CS due to other medical conditions | 5 | 4.3 |
| CS due to placenta praevia | 4 | 3.4 |
| CS due to breech presentation | 3 | 2.6 |
| Missing data | 20 | 17.2 |
| **Birth complications** | | |
| Uncomplicated | 72 | 62.1 |
| Birth asphyxia | 21 | 18.1 |
| Meconium staining | 2 | 1.7 |
| Complicated delivery-other | 5 | 4.3 |

## Physical Features

Eleven patients (17.5%) had a head circumference above the 97th percentile and only 1 (0.9%) patient had a head circumference below the 3rd percentile at presentation. Seven children (6.2%) had documented facial *dysmorphism.* Neurocutaneous markers of hypo-pigmented lesions were documented in 4 children (3.5%), and 13 children (11.5%) had hyper-pigmented lesions but none was thought to represent a syndromic or neurocutaneous disorder [17].

## Family History

A total of 62 children (53%) in the ASD cohort were the first-born children in the family. Two (3%) patients had an immediate family member and 12 (10%) had a second or third-degree relative known to have ASD. Epilepsy was reported in 2 (1.7%) family members, while 62 (53.4%) patients reported good health in the family.

## Comorbidities

Attention deficit hyperactivity disorder was the most common psychiatric comorbidity in this cohort (*n* = 24, 21%), with epilepsy in 23 (20%) children. Sleep disorders was reported in 14 (12.1%) children while elimination disorder (*encopresis or enuresis*) was reported in 12 (10.3%) children. Data on anxiety and intellectual disability was not available.

## Medication Use

A total of 46 (39.7%) children had medications prescribed as part of their management. This included sodium valproate for 19 (16%), clonazepam for 9 (8%), and clobazam for 4 (3%) for children with epilepsy. Methylphenidate was prescribed for 6 (5%) children with ADHD, while melatonin was availed for 5 (4%) and risperidone for (3%) children who predominantly presented with difficulty in initiating sleep and aggressive behavior respectively.

## Educational Status

Because most children 95 (81.9%) in this cohort were 6 years or younger at presentation, it was difficult to describe formal educational status as many were too young to have begun primary education.

However, among those who had attained school-going age (6 years and above) at presentation, 17 out of 29 (59%) children did not attend school due to lack of appropriate placement required to meet the child's needs. A total of 50 (43%) respondents were eventually enrolled in schools.

Among these, parents of 18 (36%) reported that their children had difficulties understanding what was taught in school. Half, 9 (18%) were enrolled in a mainstream school and the other half attended schools that provided learning support.

## M-CHAT-R

A total of 31 (26.7%) children aged 16 to 30 months completed the M-CHAT-R. Details of this evaluation are provided in *Table 3.* All patients who completed the M-CHAT-R also met DSM-5 criteria for ASD.

***Table 3:*** *Screening of Patients (n=31) below 36 Months of Age Using M-CHAT-R Screening Tool*

| Level of risk | N | % |
|---|---|---|
| **Low risk (0-2 risk responses)** | 0 | 0 |
| **Medium risk (3-7 risk responses)** | 15 | 48 . 4 |
| **High risk (8-20 risk responses)** | 16 | 53.3 |

## Neuroimaging

A total of 32 patients (27.5%) had MRI of the brain, of whom 12 (38.7%) had abnormal findings. All had varying degrees of white matter *hyperintensities* (WMH), though none of these were associated with restricted diffusion (***see Table 4***). Six (18.8%) of these subjects had unilateral WMH in the frontal lobe, while three had (9.4%) bilateral frontal WMH.

Four of the patients with WMH had speech delay. All six patients with unilateral WMH in the frontal lobe presented with comorbidities including developmental delay and seizures. One patient had atrophy of *corpus callosum,* another had *hemimegalencephaly.* Atrophy of the frontal lobe and perisylvian *operculum* region was reported in one child while another had *craniofacial* disproportion and *microcephaly.*

The remaining

*n* = 20 (62.5%)

patients who had an MRI did not have remarkable findings.

***Table 4***: *Patient Characteristics and Findings on MRI Brain*

| Age (Months) | Sex | WMH Region | Chief Complaint | Psychiatric Comorbidities | Epilepsy |
|---|---|---|---|---|---|
| 71 | M | Bilateral Frontal | Speech Delay, Hyperactivity, Learning Difficulty | ADHD | Y |
| 52 | M | Right Centrum Semi Ovale | Speech Delay, Concentration Difficulty, Aggression | ADHD | N |
| 84 | M | Bilateral frontal | Speech Delay | Elimination Disorder | N |
| 30 | F | Right Frontal | Speech Delay, Hyperactivity | ADHD | N |
| 115 | F | Right Lentiform Nucleus | Speech Delay, Hyperactivity, Aggression | ADHD, Sleep Disorder | N |
| 69 | M | Subcortical | Speech Delay | None | N |
| 52 | M | Bilateral Frontal | Speech Delay, Hyperactivity, Motor Deficit, Concentration Difficulty | None | N |
| 48 | M | Bilateral Peritrigonal | Speech Delay, Hyperactivity | Other NDD | N |
| 72 | M | Left Frontal | Myoclonic Jerks | ADHD | Y |
| 48 | M | Left Frontal Subcortical, Bilateral Centrum Semiovale | Speech Delay, Hyperactivity | ADHD | N |
| 32 | M | Left Frontal Subcortical | Speech Delay | Sleep Disorder | Y |
| 16 | M | Corpus Callosum | Speech Delay, Jerky movements | Elimination Disorder | Y |

***WMH** = White Matter Hyperintensities, ***NDD** = Neurodevelopmental Disorder,
***ADHD** = Attention Deficit/Hyperactivity Disorder.

## Discussion

This study, a hospital-based cohort of young children diagnosed with ASD has identified clinical similarities and some differences in comparison with other cohorts, both from sub-Saharan Africa and high-income countries (HIC).

The median age at presentation to this neurology clinic was three years, which was considerably younger than other African cohorts, in which children had diagnosis of ASD at a median age of eight years. [10, 20-24] This median age in the present Kenyan cohort is similar to the median age at diagnosis for children in the USA. The difference at age of presentation in this cohort and that from other SSA countries might be related to the socio-economic and educational status of the families that sought services at this institution. Whereas various factors including lack of awareness and stigma have been identified as contributing factors to late diagnosis of ASD in SSA, these issues could have had a smaller impact on this study. The availability of diagnostic services at this hospital might also have facilitated earlier diagnostics [23 - 25].

There were more male than female patients at a ratio of 4.3:1 in this cohort. This was consistent with data [4, 20] from other settings such as Nigeria and Denmark. Similar to other studies from SSA, expressive language delay was present in a majority of the patients in this Kenyan cohort and was more common than receptive language delay. [9, 24]

Whereas this cohort can be assumed to have had access to more resources given their higher socio-economic status, only half of these respondents

had attended a speech therapy service. There was an extremely small number of practicing speech therapists in Kenya due to lack of local training, which may explain the low proportion receiving speech therapy.

Although prenatal, perinatal, and neonatal complications, as well as pre-term and post term births, had shown to occur more frequently in populations with ASD in comparison to populations without ASD [16, 26-31], majority of respondents reported uncomplicated, vaginal births at term. This observation would need to be explored further in larger population studies or cohorts from SSA.

The occurrence of WMH, especially in the developing brains of children, has been significantly related to cognitive and functional impairment. [13 - 15] The presence of WMH in this cohort may be related to potential academic challenges as indicated by difficulty coping with school. While only one subject in this cohort demonstrated an abnormal *corpus callosum*, this was earlier found to be a common abnormality associated with ASD. Atrophy of the *corpus callosum* had been associated with delayed processing speeds as well as deficits in executive function. [13, 14]

Overall MRI brain imaging in this cohort did not contribute to the determination of etiology or association with the level of severity of ASD and would probably not be an essential investigation in a large scale study, even in this context with its higher prevalence of infectious diseases and other possible environmental contributions to ASD etiology and phenotype.

The primary limitation of a cross-sectional, chart review study was that, general ability to a larger population was limited. We were therefore not able to determine how well the characteristics of this hospital-based cohort represented the overall population in Kenya or SSA.

Kenya is characterized by rich cultural and linguistic diversity, and future studies are indicated to evaluate characteristics of representative cohorts.

This sample was potentially reflective of a population of higher socio-economic status, as the sample was drawn from a cohort seeking services at a private hospital. Though this was not measured directly.

Further, we did not have direct measures of intellectual functioning, which has important diagnostic and treatment planning implications. This should be an included focus in future studies.

Finally, a diagnosis was determined based on clinical interviews alone. Although the diagnosis was made by highly trained and experienced physicians, additional approaches using standardized instruments would have increased the validity of diagnostic determination and allowed for better comparison with prior research.

## Conclusion

This study described the clinical features of a cohort of children with a diagnosis of ASD in SSA which are similar to those in High Income Counties (HICs). Expressive language delay was observed in the majority of this cohort with less than half reporting access to necessary interventions to improve outcomes. Extending clinical investigations to representative samples, as well as including formal assessment of intellectual functioning was an important area for future studies on children with ASD in the African context.

## Disclosures

The authors declare that, they have no competing interests.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## Legends

***Table 1:*** Demographic characteristics and summary of presenting complaints, *n*=116

***Table 2:*** Maternal factors and birth history, (*n*=116)

***Table 3:*** Patient characteristics and findings on MRI Brain, *n*=32.

***Figure 1:*** Bar graph illustrating acquisition of linguistic developmental milestones in children with autism.

## List of Abbreviations

**ADHD :** Attention Deficit Hyperactivity Disorder
**ASD:** Autism Spectrum Disorder.
**DSM 5:** Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.
**ICD 10:** International Classification of Disease, *version 10.*
Kgs Kilograms.
**M-CHAT:** Modified Checklist for Autism in Toddlers.

| | |
|---|---|
| **MRI** | Magnetic Resonance Imaging. |
| **NDD** | Neuro Developmental Disorder. |
| **NHIF** | National Hospital Insurance Fund. |
| **SSA** | Sub-Saharan Africa. |
| **WMH** | White Matter Hyperintensities. |


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## Declarations

### Ethics Approval and Consent To Participate

This study was subjected to a full scientific and expedited ethics review. The Aga Khan University Hospital Ethics Committee gave the approval to conduct the study (reference number 2016/REC-50 (vl) dated 17th October 2016).

### Competing interests

The authors declare that they have no competing interests.

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