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Attention deficit hyperactivity disorder among children with sickle cell anaemia seen at the University of Benin Teaching Hospital, Benin City, Nigeria

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Abstract: *Background*
Attention Deficit Hyperactivity Disorder (ADHD) is a disorder involving persistent and impaired levels of hyperactivity, impulsiveness and lack of attention associated with impairment in executive functioning of affected children. Diagnosis of ADHD in the background of sickle cell anaemia (SCA), a haemoglobinopathy associated with neurological complications may result in significant impairment of the child into adulthood, if not detected early. In view of the fact that ADHD can be managed if diagnosed early prompted the undertaking of this study.
Subjects and Methods: Study was conducted at the Paediatric Haematology Clinic of the University of Benin Teaching Hospital, Benin City. Parents of children with SCA were informed of the study and consent obtained. Demographic characteristics were recorded. Data collection instrument was the Parent Version of the National Institute for Children's Health Quality (NICHQ) Vanderbilt ADHD Diagnostic Rating Scale (VADRS). Scoring was done for each participant using the scoring instructions for NICHQ VADRS following the *DSM-IV* criteria.
Results: A total of 103 children with SCA participated in this study. Sixty-two (60.2%) were males while 41 (39.8%) were females. Prevalence of ADHD was 15 (14.6%) with predominantly inattentive sub-type being the commonest. Children with stroke are two times more likely to develop ADHD than those without stroke (Fisher's exact test = 0.269, 95% CI= 0.589 to 7.558, Odds Ratio=2.55). Age, sex and socioeconomic status did not significantly affect the diagnosis of ADHD.
Conclusion: Prevalence of parent-reported ADHD in children with SCA is high, especially in SCA children with stroke than those without stroke.

Keywords: Attention Deficit Hyperactivity Disorder, Sickle cell anaemia, Children.

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is a complex syndrome of impairments in developmental unfolding of the unconscious self-management system of the brain that affects significant numbers of children, adolescents and can progress into adulthood.[1] It is a disorder involving persistent and impaired levels of hyperactivity, impulsiveness, and lack of attention. Diagnosis of ADHD is based on fulfilling a set of criteria using the Diagnostic and Statistical Manual (DSM). The patient has to demonstrate maladaptive symptoms inconsistent with developmental level, persisting for at least six months, of either inattention or hyperactivity-impulsivity. Some of these impairments must be present before the age of seven and must occur in two or more settings (for example, at school and at home). Also, there should be clear evidence of clinically significant impairment in social, academic or occupational functioning and there should be no other mental disorder in the child to explain these symptoms. Six or more of the 9 symptoms for inattention or hyperactivity-impulsivity is required along with other key criteria to make a diagnosis of ADHD.[1-2] The predominant subtype is ADHD subtype while the ADD subtype is rare (about 2%). Over 70% of pre-schoolers with ADHD will have at least one co-morbid neurological condition.

Sickle cell anaemia (SCA) is a genetic disease with several disease subtypes and varied symptomatology. Symptoms of the disease result from the effects of vaso-occlusion, chronic haemolysis, infections and other mechanisms with vaso-occlusion being the commonest pathophysiologic event.[3] Children with SCD are at risk

of several neurological, developmental and psychosocial complications. These complications significantly modify the conduct and activities of these children with resultant behavioural changes. Neurodevelopmental disorders such as ADHD, intellectual disability and specific learning disabilities have been documented in those in SCD.[4-6] Cerebrovascular accident (CVA) is the commonest neurological complication of SCA.[7] Other neurological complications can occur in SCA irrespective of the presence of an overt stroke.[8-10]

In the United States, the currently accepted rate for ADHD is about 5 – 10%.[1] About 35 – 65 % of children with ADHD will continue to have the disorder in adulthood. Boys are 2.4 – 4 times more likely to have the ADHD than girls.[1,11-12] In Nigeria, Amuabunos et al[13] reported a prevalence of 7.6% in normal children without SCA in the South-south zone of Nigeria while a prevalence of 3.2% was found in South Eastern Nigeria.[14] In children with SCD, there is a dearth of literature on the prevalence of ADHD. Acquazzino et al[6] found a prevalence of 25% among children with SCD referred for neuropsychological evaluation because of concerns regarding school performance, development, and/or behaviour. Similarly, Nabors and Freymuth[5] also documented a significant difference in attention between children with sickle cell disease (with or without stroke) and healthy controls.

The presence of ADHD in a child with SCA may aggravate cognitive impairment and general neurological outcome in such children. Hence, early diagnosis and appropriate treatment of ADHD may reduce the impact of the disorder on the quality of life of affected children and individuals in later life.[1] Hence, this study was conducted to determine children with SCA who have ADHD with a view for further neuropsychological testing of the positive cases.

Materials and methods

The study was conducted at the Paediatric Haematology Clinic of the University of Benin Teaching Hospital, Benin City, Nigeria. On hundred and three (103) children with SCA in steady state were consecutively recruited for the study. Parents were informed of the study and consent sought to participate in the study. Ethical approval was sought from the Ethics and Research Committee of the hospital. Data on demographic characteristics of the children was recorded. Socioeconomic class was determined using the method described by Oyedeji et al.[15] The instrument used was the Parent Version of the National Institute for Children's Health Quality (NICHQ) Vanderbilt ADHD Diagnostic Rating Scale (VADRS).[16] It is a psychological assessment tool validated for diagnosing ADHD and the effects on behaviour and academic performance in children aged 6–12years following fulfilment of DSM IV-TR requirement for diagnosis of ADHD.[16] However, in collecting information to establish Diagnostic and Statistical Manual of Mental Disorders criteria, they are applicable to other groups, particularly preschoolers, where it has been identified that *DSM-IV* criteria are still appropriate.[16] The instrument was administered to the parents by the researcher and research assistants. Scoring was done for each participant using the scoring instructions for NICHQ VADRS.[16]

Data obtained was imputed and analyzed using IBM-SPSS Version 26. Categorical variables were presented as frequencies and proportions while continuous variables were represented as means (±SD). Chi-square was used to determine the association between categorical data while analysis of variance (ANOVA) was used to compare means. The statistical significance was set at p=<0.05 at 95% confidence interval (CI).

Results

Bio-Data

A total of 103 children with SCA aged 1-17 years participated in this study. Sixty-two (60.2%) were males while 41 (39.8%) were females. The male: female ratio 1.5: 1. All the children were haemoglobin SS and none were on medication for ADHD. Forty-six (44.7%) were from high socioeconomic class. Classification of subjects into age groups is shown in Table 1.

Table 1: Socio-Demographic Characteristics of Study Subjects

Characteristics	Frequency	Percentage (%)
Sex		
Male	62	60.2
Female	41	39.8
Social class		
Upper	46	44.7
Middle	28	27.2
Lower	29	28.1
Age group (years)		
1 - 5yrs	26	25.2
6 - 12yrs	48	46.6
13yrs and above	29	28.2

Prevalence of ADHD and sub-types

The prevalence of ADHD (Combined Inattention/ Hyperactivity) was 14.6% with 15 out of 103 children fulfilling the criteria for ADHD (95% CI= 8.8 – 22.3%). Of those with ADHD, 8 (53.3%) had predominantly inattentive sub-type while 1 (6.7%) had predominantly hyperactive/impulsive subtype (Table 2).

Table 2: Subtypes/Domains of ADHD

Subtypes/Domains of ADHD	Frequency (%)	95% CI
Predominantly Inattentive (ADHD-I)	8 (53.3)	29.4-76.1%
Predominantly Hyperactive/ Impulsive (ADHD-HI)	1 (6.7)	0.7-27.2%
ADHD Combined Inattention/Hyperactivity (ADHD-C)	6 (40.0)	18.8– 64.7%

Factors affecting diagnosis of ADHD

Age, gender and socio-economic status of subjects did not significantly affect the diagnosis of ADHD, Table 3.

Socio-demographic characteristics and sub-types of ADHD

Table 4 shows the socio-demographic characteristics of the specific sub-types of ADHD. Boys were more affected with all sub-types of ADHD than girls but the difference was not statistically significant. There was no significant difference in age-group and socio-economic class and the sub-types of ADHD.

Table 3: Factors affecting diagnosis of ADHD

Characteristics	Frequency	Percentage (%)	c^2	P
Age (Years)				
1-5	4	15.4	0.028	1.000
6-12	7	14.6		
13 and above	4	13.8		
Sex				
Male	12	19.4	2.874	0.090
Female	3	7.3		
Social Class				
Upper	6	13.0	0.343	0.880
Middle	5	17.9		
Lower	4	13.8		

Table 4: Socio-demographic Characteristics of ADHD Sub-types

Characteristics	ADHD-I n (%)	ADHD-HI n (%)	ADHD-C n (%)	c^2	P
Age (Years)					
1-5	3(75.0)	0(0.0)	1(25.0)	4.688	0.321
6-12	2(28.6)	0(0.0)	5(71.4)		
13 and above	3(75.0)	1(25.0)	0(0.0)		
Sex					
Male	6(50.0)	1(8.3)	5(41.7)	0.417	0.812
Female	2(66.7)	0(0.0)	1(33.3)		
Social Class					
Upper	3(50.05)	0(0.0)	3(50.0)	2.860	0.860
Middle	3(60.0)	1(20.0)	1(20.0)		
Lower	2(50.0)	0(0.0)	2(50.0)		

ADHD in SCA children with stroke

Of the seven children with SCA with stroke, 2 (28.6%) had ADHD. Prevalence of ADHD in children with stroke was higher than in those without stroke but the difference was not significantly higher (Fisher's exact test = 0.269, 95% CI= 0.589 to 7.558, Odds Ratio=2.55).

Discussion

The prevalence of ADHD among children with SCA in this study was 14.6%. This prevalence is lower than the 25% prevalence reported by Acquazzino *et al*[6] among children with SCD referred for neuropsychological testing due to concerns regarding school performance, development and/or behaviour.[6] The lower prevalence found in this study may be due to the fact that majority of the children recruited have no background neuropsychological concerns or testing done while the study by Acquazzino et al[6] was primarily carried out on children specifically referred for neuropsychological testing who are more likely to have background neurological abnormalities like ADHD and others. Prevalence of ADHD found in this study is higher than 8% documented in a community study by Ofovwe *et al*[17] and 7.6% by Amuabunos et al[13] for normal children in same locale as this study. A lower prevalence of 3.2% was also reported in a hospital based study of normal children by Chinawa et al[14] in South Eastern Nigeria while 8.7% was documented by Adewuya *et al*[18] in Ilesa, South West, Nigeria. This higher prevalence found among children with SCA is not surprising because children with SCA are prone to neurological events such as stroke and silent infarcts that can result in cognitive dysfunctions and other central nervous system abnormalities.[19-22] The effect of chronic hypoxia on the brain vis a viz cognitive dysfunction and behavioural abnormalities has also been documented in SCA.[21-22]

Males were more likely to have ADHD than females in this study. This is consistent with what has been documented by other studies in the general population.[1,23] This is not surprising because boys are usually more physically active than girls and this increased physical activity may aggravate the symptoms of ADHD in boys. About half of the children with SCA who had ADHD were within the ages of 6-12 years. Before 6 years of age, most impulsive actions and inattention may be regarded as normal behaviours for the developmental age of the child.[24] The 6-12 years age bracket which is the school-age period is a time when the effects of lack of inhibition and effects of impulsivity and inattention become more obvious.[1] Most prevalence studies were done in this age-group and the American Academy of Pediatrics (AAP) recommended DSM-IV particularly for this age-group.[1,13] The prevalence of ADHD in pre-schoolers is comparable to inci- dence rates among schoołaged children (2 – 6%) in the US.[1] Hence, it has been suggested that DSM-IV criteria can also be used to assess ADHD in other age-groups especially in pre-schoolers.

Among the sub-types of ADHD, predominantly inattentive sub-type (ADHD-I) was the commonest in over half of the patients. This is similar to what Amuabunos et al[13] found among the general population in the same locale. Similarly, Chinawa et al[14] had the same finding in another geo-political zone of the country. Across all the age groups, ADHD-I was the commonest sub-type, followed by ADHD-C in this study. This is contrary to reports from the United States where it was thought that in pre-schoolers, ADHD-HI is the prevalent sub-type while ADHD-I is rare.[1] It has been noted that the features of inattention gets noticed when children begin

schooling; when reading and independent work are required.[1] However, most parents in this study reported that their pre-schoolers were inattentive. Pre-schoolers are known to have short attention span[24] and may easily be termed inattentive; hence this may have affected the reports of parents regarding their children.

Among SCA children with stroke, prevalence of ADHD was higher than in those without stroke, although the number of children with stroke in this study is few. There is two-times likelihood of having ADHD in the presence of stroke. Stroke is the most common and most severe neurological complication of SCA.[7,19] Other complications such as behavioural disorders, cognitive dysfunction and learning disabilities have been described in the setting of SCA.[20-22,25] Thus, it is not surprising that the presence of stroke contributed significantly to the development of ADHD in this study. Age, sex and socio-economic status of the subjects did not significantly affect the diagnosis of ADHD in this study. This suggests that socio-demographic factors may not be associated with development of ADHD. Other studies[13,14] also documented similar findings with regards to socio-demographic characteristics in the general population.

Conclusion

The prevalence of parent-reported ADHD in children with SCA is higher than prevalence reported in the general population. Prevalence is significantly higher in those SCA children with stroke than those without stroke. Further detailed evaluation, treatment and follow-up of these children will reduce the problems that may arise from untreated ADHD.

Contributions of Authors
Okunola Peter O: Was involved in conceptualization of work and writing of the article.
Israel-Aina Yetunde T: Was involved in conceptualization, coordinated data collection, data analysis and writing of the article.
Aina Israel O: Was involved in conceptualization, worked on the measurement instrument and writing of the article.
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References

1. Hanna N. Attention Deficit Disorder (ADD), Attention Deficit Hyperactive Disorder (ADHD): Is it a product of our modern lifestyles? American Journal of Clinical Medicine. 2009; 6 9(2), 21-28.
2. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th Edition. Text Revision. Washington DC, American Psychiatric Association, 2000.
3. Adewoyin AS, Management of Sickle Cell Disease: A Review for Physician Education in Nigeria (Sub-Saharan Africa). Anemia; 2015: Article ID 791498, 21 http://dx.doi.org/10.1155/2015/791498)
4. Lance EI, Comi AM, Johnston MV, Casella JF, Shapiro PK. 12
5. Michael V. Johnston 1Kennedy Krieger Institute, Baltimore, MD, USA 2 Johns Hopkins University School of Medicine, Baltimore, MD, USA
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6. Risk Factors for Attention and Behavioral Issues in Pediatric Sickle Cell Disease. *Clin Pediatr. 2015; 54(11): 1087–1093.*
7. Nabors NA, Freymuth AK. Attention deficits in children with sickle cell disease. *Percept Mot Skills. 2002; 95(1): 57-67.*
8. Acquazzino MA, Miller M, Myrvik M, Newby R, Scott JP. Attention Deficit Hyperactivity Disorder in Children With Sickle Cell Disease Referred for an Evaluation. *J Pediatr Hematol Oncol. 2017; 39 (5): 350-354.*
9. Ohene-Frempong K, Weiner SJ, Sleeper LA, et al. Cooperative Study of Sickle Cell Disease. Cerebrovascular accidents in sickle cell disease: rates and risk factors. *Blood. 1998; 91:288–294.*
10. Berkelhammer LD, Williamson AL, Sanford SD, et al. Neurocognitive sequelae of pediatric sickle cell disease: a review of the literature. *Child Neuropsychol. 2007; 13: 120–131.*
11. Steen RG, Fineberg-Buchner C, Hankins G, Weiss L, Prifitera A, Mulhern RK. Cognitive deficits in children with sickle cell disease. J Child Neurol. 2005; 20: 102–107.
12. Vichinsky EP, Neumayr LD, Gold JI, et al. Neuropsychological Dysfunction and Neuroimaging Adult Sickle Cell Anemia Study Group. Neuropsychological dysfunction and neuroimaging abnormalities in neurologically intact adults with sickle cell anemia. *JAMA. 2010; 303: 1823–1831.*
13. Prevalence of Parent-Reported ADHD Diagnosis and Associated Treatment among U.S. Children and Adolescents, 2016. Melissa L. Danielson, MSPH1; Rebecca H. Bitsko, PhD1; Reem M. Ghandour, DrPH2; Joseph R. Holbrook, PhD1; Michael D. Kogan, PhD2; Stephen J. Blumberg, PhD3. Journal of Clinical Child and Adolescent Psychology. Published online before print January 24, 2018.

14. General Prevalence of ADHD. Available at: https://chadd.org/about-adhd/general-prevalence/ Accessed on 09/04/2021.
15. Amuabunos EA, Ofovwe EG, Ibadin MO,Community survey of attention-deficit/ hyperactivity disorder among primary school pupils in Benin City, Nigeria, *Annals of African Medicine*. 2011; 10 (2): 91–96.
16. Chinawa JM, Odetunde OI, Obu HA, Chinawa AT, Bakare MO, Ujunwa FA. Attention Deficit Hyperactivity Disorder: A Neglected Issue in the Developing World. Behavioural Neurology; 2014. Article ID: 694764 | 6 pages | https://doi.org/10.1155/2014/694764.
17. Oyedeji GA. Socio-economic and cultural background of hospitalized children in llesha. *Nigeria Journal of Paediatrics, vol. 12, pp. 111–117, 1985.*
18. NICHQ Vanderbilt Assessment Scales (Archived). American Academy of Pediatrics, McNeil. Available at: https://www.nichq.org/resource/nichq-vanderbilt-assessment-scales. Accessed on 09/04/2021.
19. Ofovwe C, Ofovwe GE, Meyer A. The prevalence of attention-deficit/hyperactivity disorder among school- aged children in Benin City, Nigeria. *J Child and Adolescent Mental Health 2006; 18(1): 1-5.*
20. Adewuya AO and Famuyiwa OO. Attention deficit hyperactivity disorder among Nigerian primary school children Prevalence and co-morbid conditions. *European Child & Adolescent Psychiatry. 2007; 16: 10-15.*
21. DeBaun MR, Schatz J, Siegel MJ, et al. Cognitive screening examinations for silent cerebral infarctions in sickle cell disease. *Neurology 1998; 50: 1678–1682*
22. Lobo C, Moura P, Rio P, Maia H, Fernandes J, Pinto JC. Cognitive Dysfunction Occurs In Children with Sickle Cell Anemia without Cerebral Ischemic Insult or Vasculopathy. *Blood. 2011; 118 (21): 1076.*
23. Steen RG, Xiong X, Mulhern RK, Langston JW, Wang WC. Subtle brain abnormalities in children with sickle cell disease: relationship to blood hematocrit. *Ann Neurol 1999; 45: 279–286*
24. Brown RT, Buchannan I, Doepke K, et al. Cognitive and academic functioning in children with sickle cell disease. *J Clin Child Psychol 1993; 22: 207–218*
25. Umar MU, Obindo JT, Omigbodun OO. Prevalence and Correlates of ADHD among Adolescent Students in Nigeria. Journal of Attention Disorders. 2015; 22: 116-126
26. Nelson's Textbook of Pediatrics 21st edition. Kliegman R, Stanton B, St. Geme J, Schor N (eds). Elsevier, Philadelphia, 2020.
27. Israel-Aina YT and Okunola PO. Behavioural changes in children with sickle cell disease in Benin City, Nigeria. *Annals of Biomedical Sciences. 2019; 18: 121-125.*