NEURODEVELOPMENTAL OUTCOMES OF PRESCHOOL-AGE CHILDREN WITH COMORBID SICKLE CELL DISEASE AND AUTISM SPECTRUM DISORDER

DEPARTMENT OF AUDIOLOGY, SPEECH AND LANGUAGE THERAPY

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THIS DISSERTATION IS SUBMITTED TO THE UNIVERSITY OF GHANA, LEGON IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE AWARD OF MSC IN SPEECH AND LANGUAGE THERAPY DEGREE

JANUARY 2023

DECLARATION

I, the undersigned, hereby declare that this dissertation which is being submitted in fulfilment of the requirements for the Master of Science Degree in Speech and Language Therapy is the result of my own research undertaking under supervision, and that, with the exception of other sources and references duly cited, this work is original research which has not been previously presented for another degree.

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DEDICATION

'I will speak for you, I will fight for you, I will advocate for you so that one day you can do it for yourself' - anonymous

This dissertation is dedicated to my children, Benji Michael whose diagnosis of autism spectrum disorder chartered this course for me, and to my phenomenal daughter, Kiara-Joy, my greatest motivator whose undying passion to join me help her brother and other neurotypical children has kept this flame burning bright.

ACKNOWLEDGEMENT

'I've learned that people will forget what you said, people will forget what you did, but people will never forget how you made them feel.'- Maya Angelou

I am forever thankful to God for helping and guiding me throughout this arduous journey.

To my supervisors and anchors, A/Prof Samudragupta Bora for your unquantifiable input, dedication and belief in me, and to Ms Victoria Nana Akua Owusu whose prayers and timely words of encouragement have all led to the success of this dissertation. I am very thankful to you both.

My gratitude also goes to my Head of Department and all the fine lecturers who tutored me. Your personal interest in my well-being kept my head above the waters.

To my mum-my woman of substance and lead cheerleader, to my father, siblings, Amma Dankwa and Rebecca Kuma my heart is bursting with gratitude for your unending encouragement and support.

My gratitude also goes to Eugene A. Kwarteng, Mr. and Mrs. Biney-Oyibi, Dr Aryee (Biochemistry Department-Korle-Bu), Mr. Clement Amponsah and to Dr Seth Asafo, I couldn't have made it without your immense contribution to my personal and academic life.

My gratitude goes to Prof Daniela O'Neill, author of the Language Use Inventory at the University of Waterloo, Ontario, Canada for providing free access to the copyrighted instrument and their online platform, and to Dr. Brew, Head of Paediatrics, Greater Accra Regional Hospital for your immense contribution to this study. My gratitude also goes to the West African Genetic Medicine (WAGMC) for your scholarship.

To everyone I met on this journey, my heartfelt gratitude goes to you all for setting me on a path of success.

ABSTRACT

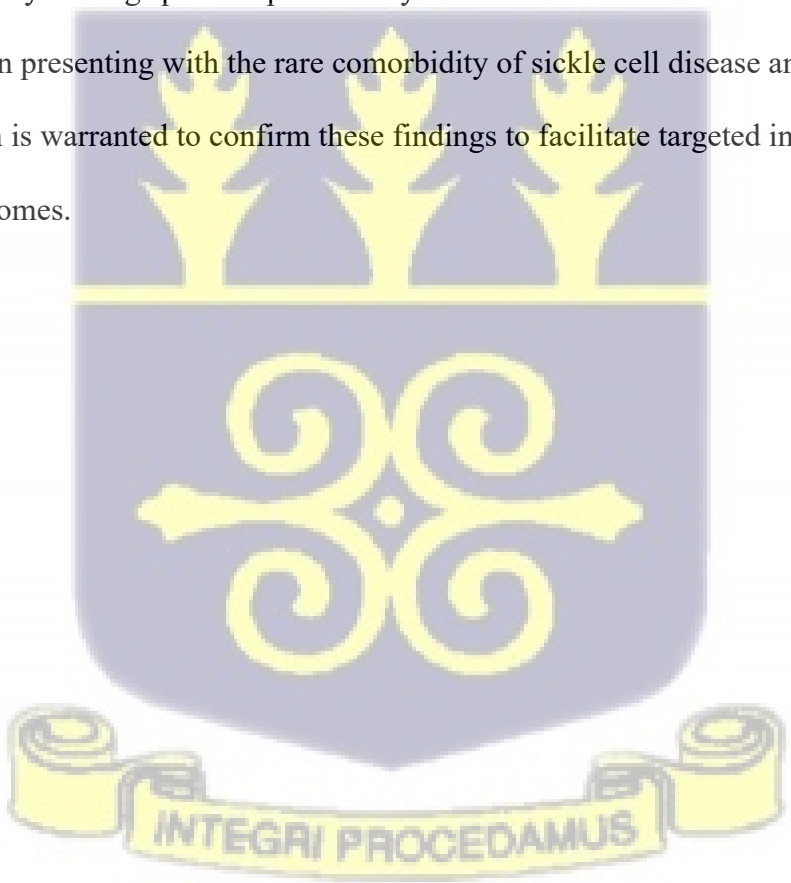
Aim: There are some overlaps in the childhood neurodevelopmental profiles of sickle cell disease and autism spectrum disorder. Nonetheless, there is limited evidence on the neurodevelopmental outcomes of children with comorbid sickle cell disease and autism spectrum disorder. Thus, the aim of this pilot study was to examine preschool-age neurodevelopment including social communication skills of children with a comorbid diagnosis of sickle cell disease and autism spectrum disorder, relative to children with a diagnosis of sickle cell disease only, autism spectrum disorder only, and typically developing children.

Methods: Using a cross-sectional research design and convenience sampling, 65 preschool-age children were enrolled in this study: 20 participants in each of the three study groups and 5 in the comorbid group. Child outcomes were assessed using standardized parent-rated questionnaires following informed consent. Ages & Stages Questionnaires®, Third Edition (ASQ®-3) was used to screen neurodevelopment across the domains of communication, gross motor, fine motor, problem solving, and personal-social, and the Language Use Inventory screened social communications across the domains of usage of gestures, words, and longer sentences. Regarding data analysis, first, the Chi-squared test of independence was used to compare sample characteristics between groups. Second, one-way ANOVA was used to compare scores on the ASQ®-3 domains and the Language Use Inventory between groups, followed by posthoc tests for significant variables. A p-value of less than 0.05 was considered statistically significant.

Results: No significant baseline differences were evident across the four study groups for gender (p=.11), hearing impairments (p=.91), vision impairments (p=.73) as well as maternal sociodemographic characteristics (p>.05). There were no significant differences in the mean

scores of any of the ASQ®-3 domains (p>.05) for children with comorbid sickle cell disease and autism compared with autism alone. However, children with comorbid sickle cell disease and autism had significantly lower scores on communication (p<.001), problem solving (p=.008), and personal-social (p<.001) domains than children with sickle cell disease only. Regarding social communication, while the comorbid and non-comorbid groups did not differ significantly in their usage of gestures (p>.05), there was a significant between-group difference in their word usage (p<.05), Further, children with comorbid sickle cell disease and autism had significantly lower scores on their usage of longer sentences than children with sickle cell disease only (p=.002).

Conclusion: Study findings provide preliminary evidence of elevated neurodevelopmental risks for children presenting with the rare comorbidity of sickle cell disease and autism. Further research is warranted to confirm these findings to facilitate targeted interventions for optimizing outcomes.



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LIST OF ABBREVIATIONS

ADHD	Attention Deficit Hyperactivity Disorder
ASD	Autism Spectrum Disorder
ASQ®-3	Ages and Stages Questionnaire Third Edition
LUI	Language Use Inventory
NDD	Neurodevelopmental Disorder
SCD	Sickle Cell Disease

CHAPTER ONE

CONCEPTUALISING THE STUDY

1.1 Introduction

Researchers, clinicians and therapists have over the years sought to discover the nature of sickle cell disease (SCD), autism spectrum disorder (ASD) and its impacts on patients and families. While there are extensive investigations of neurodevelopment in children with SCD or ASD, there is limited focus on the group of children with comorbid SCD and ASD. Although a rare comorbidity, there is some evidence that these children may represent a highly vulnerable group for neurodevelopmental delays/deficits.

Schatz et al. (2009) investigated the language processing deficits of school-age children with SCD. They found that those with low neurological risk did not exhibit language processing deficits relative to their demographically matched peers; however, children with high neurological risk showed deficits in all the language domains tested. A major finding of this study is that language processing deficits in children with SCD at the start of middle childhood were shown to be related to neurologic risks and include language skills expanding beyond vocabulary. These findings demonstrate the need to broaden the focus of SCD early childhood research to better understand the true outcomes profile of this high-risk population.

Kjellmer et al. (2018) reported that while language impairments among children with ASD are common, knowledge of the actual nature of this disorder is limited. They noted that children with autism often find it difficult to understand and/or formulate their language to express themselves. The literature however is inconclusive; some studies have reported impaired receptive than expressive language abilities in children with autism, while others have reported the opposite. In contrast, Kwok et al. (2015) in a meta-analysis found that

receptive and expressive language may be equally impaired. Regardless, studies have shown that in children with autism, receptive and expressive language abilities vary across the intelligence spectrum and within the group of children with autism without comorbid intellectual disability. For example, Chan et al. (2005) observed impaired sentence comprehension in children with autism without intellectual disabilities. Åsberg (2010) contrastingly reported that school-age children with autism without intellectual disabilities performed as well as typically developing peers on word and sentence comprehension but had impaired narrative-discourse comprehension. Moreover, a relatively large proportion of children with autism without intellectual disabilities are likely to exhibit neither receptive nor expressive language problems.

Regarding comorbid SCD and ASD, Eboni et al. (2021) in their retrospective cohort study between July 2017 and January 2019 demonstrated that children with SCD and neurodevelopmental disorders have higher odds of having certain disease-related complications including multidimensional language problems. Likewise, Hariman et al. (1991) had earlier emphasized that neurologic disease from SCD complications manifests itself in a wide variety of syndromes, including intellectual deficits, cognitive difficulties, and reduced language function.

1.2 Problem Statement

SCD and ASD are two of the most common disorders impacting childhood neurodevelopment and the quality of life. There are limited reliable statistics on the true prevalence of these disorders in Ghana. As reported by Asare et al. (2018), approximately 2% of children in Ghana are born with SCD annually. Children born with SCD are at a high risk of developing neurological complications such as silent cerebral infarction, stroke and

cognitive deficits as well as neurodevelopmental disorders (Lance et al., 2019). Further, children with SCD demonstrate lower full-scale, verbal, and performance IQs despite having normal neuroimaging as well as higher rates of learning and intellectual disabilities and other developmental delays relative to typically developing children of the same age, race and gender (Lance et al., 2018). Equally debilitating is autism or ASD, a neurodevelopmental condition that can be detected as early as infancy (Bello-Mojeed et al., 2014). Based on recent estimates, the prevalence of ASD in Ghana is about 0.6% of the country's total population. Similarly, 1 in 87 children in Ghana under the age of 3 years is affected by this neurodevelopmental condition (Rural Integrated Relief Service-Ghana, 2010). These children are well-recognized to be at risk of poor cognitive, language and motor outcomes. Studies have shown that motor impairment increases in children with ASD as a function of social communication, cognitive and functional impairment, repetitive behaviour severity and comorbid diagnoses (Bhat, 2021).

Taken together children with comorbid SCD and ASD may represent a dual-risk group. Nonetheless, there is limited evidence of their neurodevelopmental outcomes, which is critical for the early detection of impairments and the provision of targeted early interventions to optimize outcomes and improve the child and their family's quality of life.

1.3 Aim of the Study

To examine preschool-age neurodevelopment including social communication skills of children with a comorbid diagnosis of SCD and ASD, relative to children with a diagnosis of SCD only, ASD only and typically developing children.

1.4 Specific Objectives

1) To characterize neurodevelopmental outcomes across the domains of communication, gross motor, fine motor, problem solving and personal-social among preschool-age children with a comorbid diagnosis of SCD and ASD, relative to children with a diagnosis of SCD only, ASD only and typically developing children.

2) To compare pragmatic social communication skills across the domains of the usage of gestures, words and longer sentences among preschool-age children with a comorbid diagnosis of SCD and ASD, relative to children with a diagnosis of SCD only, ASD only and typically developing children.

1.5 Justification

The childhood neurodevelopmental profiles of SCD and ASD overlap. Further, genetics have been identified as a major aetiologic factor across both clinical conditions. Nonetheless, there is a limited understanding of the neurodevelopmental outcomes of children with comorbid SCD and ASD. Although this a rare comorbidity, their early childhood neurodevelopment profiles must be established. Furthermore, the high burden of both SCD and ASD in Africa, including in Ghana, highlights the critical need to better understand their profiles within the local context. This has relevance for the early detection of neurodevelopmental impairments in this high-risk population, thereby providing opportunities for targeted intervention to optimize outcomes.

CHAPTER TWO

CONCEPTUAL FRAMEWORK AND LITERATURE REVIEW

2.1 Introduction

This chapter comprises a review of related literature on the topic under study. The neurodevelopmental outcomes of children of preschool age with SCD have received increasing scholarships and policy considerations in the past decade (Schatz et al., 2017, Downes et al., 2018, Galadanci et al., 2019, La'Kita et al, 2021, Lance et al., 2021, Heitzer et al, 2022). Also, the neurodevelopmental outcomes of preschool-age children with ASD have attracted great scholarly and policy attention in recent times (Leitner, 2014, Kantzer, 2018, Steffenburg et al., 2018, Lin et al., 2019, Papadopoulos et al., 2022, Kilicaslan & Tufan, 2022). However, there is a lack of scholarly exploration of neurodevelopmental outcomes of preschool-age children with comorbid SCD and ASD. In this line, previous research will be examined using content analysis methods to demonstrate how it has aided in comprehending the phenomenon of the subject under investigation. If there are any gaps in the literature, they will be emphasized along with any connections to how this study aims to close those gaps. The literature review section has been categorized into two main sub-sections. These include the conceptual framework and empirical reviews. The empirical reviews include perceptions of neurodevelopmental outcomes of preschool-age children, the global perspective on SCD of preschool-age children, the global perspective on ASD of preschool-age children, the Ghanaian view on SCD and ASD of preschool-age children, challenges in addressing neurodevelopmental outcomes of preschool-age children with SCD and ASD, and recommendations/existing protocols for addressing neurodevelopmental outcomes of preschool-age children with SCD and ASD will also be discussed.

2.2 Conceptual Framework

SCD is a series of inherited blood abnormalities caused by aberrant haemoglobin present in red blood cells. ASD is a group of neurodevelopmental disorders characterized by difficulties in social communication, limited interest in the environment, and stereotyped repetitive activities. The combination of these two disorders may lead to impairments in cognitive, linguistic and motor development of preschool children with SCD and autism from infancy until early childhood. Therefore, there is a need for all stakeholders including parents, governments, healthcare professionals and citizens to identify and adopt a series of mechanisms to help control and prevent the health threat.

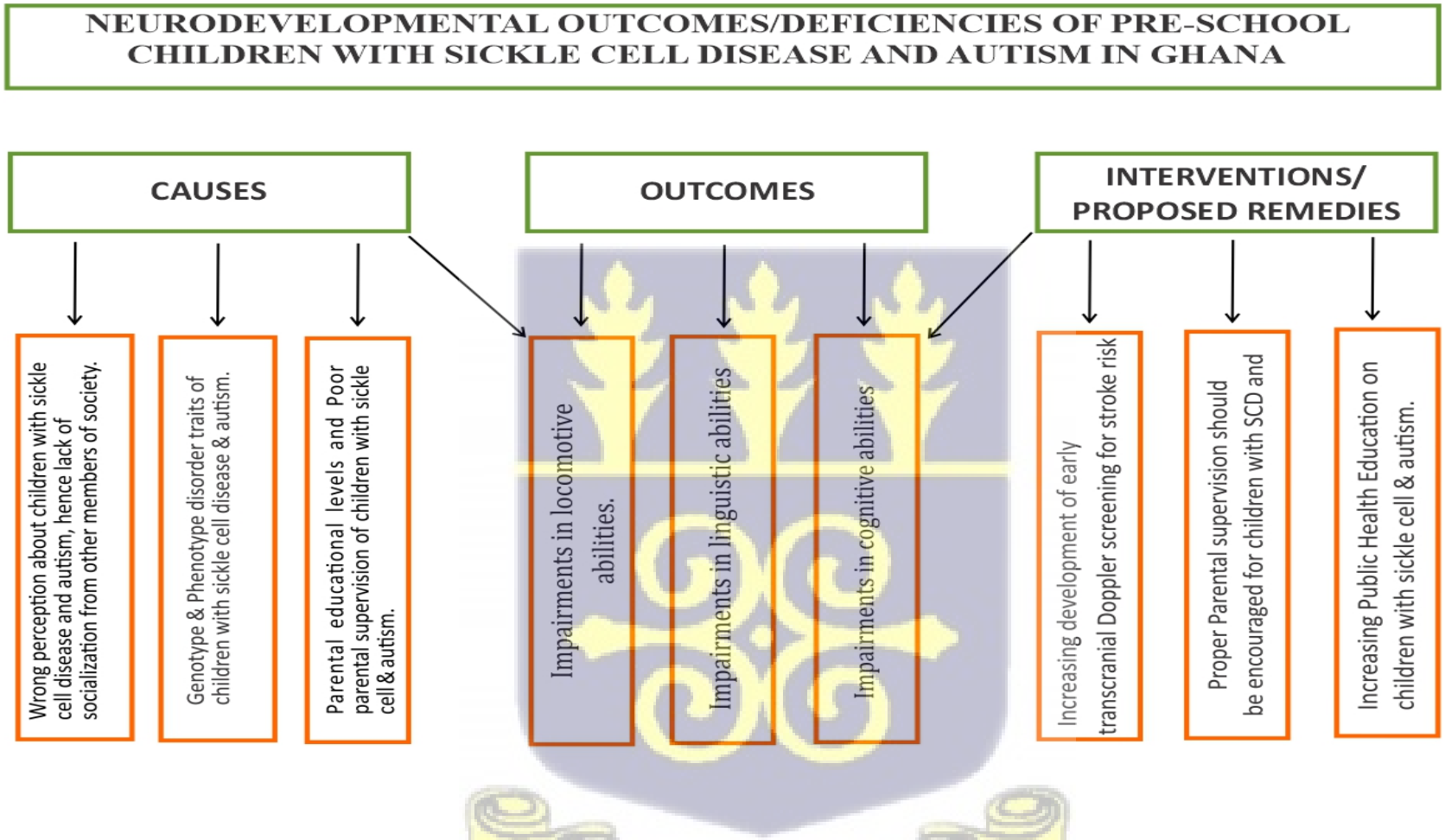


Figure 1:Proposed Conceptual Framework of Neurodevelopmental Outcomes of Preschool Children with Sickle Cell Disease and Autism in Ghana.

The framework in Figure 1 above explains that neurodevelopmental outcomes/deficiencies of preschool children with SCD and autism in Ghana may arise from a confluence of biological and social factors which include parental educational levels and poor parental supervision of children with SCD & autism, genotype & phenotype disorder traits of children with SCD & autism, wrong perception about children with SCD and autism, hence lack of socialization from other members of society, among others. These lead to slower neurocognitive, linguistic and locomotive abilities and develop as neurodevelopmental delays/deficits for children with SCD and autism.

Therefore, to address the menace, attempts should be made to prevent or control the causes or impacts, to minimize, prevent or control the prevalence of neurodevelopmental delays/deficits in preschool children with SCD and autism in Ghana.

2.3 Related Literature Reviews

2.3.1 Perceptions of Neurodevelopmental Outcomes of Preschool-Age Children

Several research studies in recent times including (Reardon & Owens, 2014, Alson et al., Boutrin & Williams, 2021, Zheng et al., 2021, Dagher & Linares, 2022) have shown that racial and/or socioeconomic disparities in a variety of exposures to upstream social factors are important for a child's development and these include parental incarceration, family poverty, residential segregation, neighbourhood violence and quality. As a result, these social variables have an impact on several environmental factors which are known to affect a child's neurodevelopment, such as the amount of cognitive stimulation, the quality of early care and education, psychosocial stress and exposure to a variety of toxins (such as lead, air pollution, phthalates, and flame retardants), (Zheng et al., 2021, Dagher & Linares, 2022).

Ryan et al (2014) assert that children are likely to show varying degrees of susceptibility depending on whether protective factors like good parenting practices, high-quality early education, and adequate nutrition are present or not, even though these unfavourable environmental exposures increase the likelihood of neurodevelopmental impairments of preschool-age children. However, Bellinger et al (2016), posit that the influence of hazardous chemical and non-chemical exposures on numerous biological and psychological processes might result in diverse functional patterns that may manifest throughout multiple neurodevelopmental domains of preschool-age children.

Also, Hyman et al. (2020), explain that given the multiple influences on numerous domains of early childhood neurodevelopment, it is necessary to consider the fundamental elements of early development simultaneously to identify subgroups of children who demonstrate common neurodevelopmental patterns. Therefore, Spittle et al (2020) indicate that parental care, demographics, socioenvironmental and biological factors influence the neurodevelopmental outcomes of preschool-age children. These include household income level, maternal demographics (such as employment status, educational attainment and relationship status), maternal mental health (such as symptom levels of stress and depression, social support, substance abuse, life orientation and experiences of domestic violence), maternal parenting characteristics (such as knowledge of effective parenting, criticism toward their child-rearing practices: nurturance and conflict) and home environment (such as social support systems, school, and neighbourhood).

In addition to the above, Li et al (2019) for instance found that males are more likely to have neurodevelopmental disorders and are more vulnerable to environmental exposures. To support the views by Li et al (2019), O'Connor et al (2020) revealed that a child's biological sex was also considered as a risk factor given that males are at greater risk of

neurodevelopmental disorders and more susceptible to environmental exposures compared to females.

The above scholarly works in this section contribute significantly to the understanding of the topic under study by revealing some biological and sociological factors which influence neurodevelopmental outcomes in preschool-age children. However, there is a dearth of scholarly exploration in assessing the neurodevelopmental outcomes of preschool-age children with comorbid SCD and ASD.

2.3.2 The Global Perspective on SCD of Preschool-Age Children

Hoyt et al (2022) define SCD as a series of inherited blood abnormalities caused by aberrant haemoglobin present in red blood cells. Both parents need to pass the abnormal haemoglobin gene on to a child for the child to develop the disease. Around 300,000 infants are born each year with SCD worldwide, with nearly 75% of these births in sub-Saharan Africa, and the majority of them die before turning five in developing nations (Hoyt et al, 2022). Narh et al., (2021) assert that evidence of the prevalence and complications of SCD in Africa, particularly in Ghana, is growing. The prevalence of the genetic tendency was 25%–30% in countries in tropical Africa (Narh et al, 2021).

Hypoxia, repetitive tissue ischemia, and cumulative micro-infarcts are examples of chronic neurological injuries associated with children with SCD (Schranz et al., 2019). This is supported by Kassim & Sharma (2017), who posit that between 25% and 35% of children with SCD experience silent infarcts. Stroke and silent infarcts are both significantly related to neurocognitive function in SCD. However, Chaturvedi & DeBaun (2016), establish that the prevalence of overt stroke in children is now below 2% due to advancements in science and

technology which has led to increasing development of transcranial Doppler screening for stroke risk and chronic transfusion therapy for those deemed at risk.

Studies have shown impairments in cognitive, linguistic and motor development from infancy until age three for children with SCD (Drazen, et al., 2016, Fields et al., 2016, La'Kita et al., 2021). DeBaun et al. (2013), revealed that from age 12 to 24 months, there was a discernible drop in cognitive development for children with SCD. However, studies have shown developmental delays in SCD that are independent of lab results or the SCD genotype (La'Kita et al, 2021). On the contrary, a more recent study by Hoyt et al. (2022) found that 2- and 4-year-olds with a more severe SCD genotype were more likely to experience developmental delays. Fields et al (2016), however, assert that reduced parental education, household income, and community resources are environmental predictors of developmental delays in children with SCD.

Leung (2021) also evaluated the neurocognitive function in preschool aged SCD patients. Their findings showed medium to large effect sizes for linguistic, visuospatial and motor domain deficiencies. In addition, Trpchevska et al (2022), carried out a study on young children with SCD by establishing the relationship between socioeconomic status and neurocognitive performance rather than lab results or genotype. The study focused on similar demographic characteristics to show how children with SCD easily find difficulties in acquiring school readiness skills, which has a tendency towards the development of language abilities. Despite the above studies, Ashouri et al., (2021) highlighted those treatments for SCD symptoms, such as hydroxyurea (HU), have demonstrated possible neuroprotective effects.

The prevalence of SCD especially in sub-Saharan Africa makes it a major public health concern since children with SCD experience neurodevelopmental delays. However, there is

little research assessing neurodevelopmental outcomes in young children and preschoolers with SCD. Also, there is limited research on neurodevelopmental outcomes of preschool-age children with SCD from the Ghanaian perspective. This research lacuna is what this study seeks to fill.

2.3.3 The Global Perspective on ASD of Preschool-Age Children

Senouci et al (2021) explain that ASD is characterized by persistent impairment in social interaction and communication as well as constrained and recurrent patterns of behaviour and interests. According to global estimates, one in 100 children globally suffers from autism (AlBatti, et al., 2022). This estimate is a typical value, and stated prevalence varies widely between studies.

According to the U.S. Center for Disease Control, 1 in 44 American children has been given an ASD diagnosis as of 2021 (Shaw et al., 2021). Among children aged 6 to 12 in China, a countrywide survey conducted in 2021 found a frequency of 0.7% of children with ASD, (Zhao et al., 2021). However, in sub-Saharan African countries, the prevalence of ASD is estimated to be 1 in 145 among children with intellectual disabilities (Maenner et al., 2021). Such high incidence rates attracted interest from around the globe. In comparison to girls, boys are four times more likely to receive an autism diagnosis (D'Mello et al., 2022).

Von Gontard et al. (2022) establish that ASD is associated with other disorders including attention deficit hyperactivity disorder (ADHD), intellectual disability and frequent physical conditions. However, Posserud et al (2022) stress that intellectual disability is significant since it is frequently present in children with ASD. Smith & Gropman (2021) revealed that in the U.S., 23.1% of 8-year-old ASD patients had scores that were borderline, and 35.2% had IQs of 70 or less.

In line with the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), individuals with ASD and intellectual disabilities have imbalanced IQ subitems (Zhang et al., 2022). In contrast to their nonverbal talents, Nicpon et al (2021) establish that their social communication and interaction skills such as fine motor skills and nonverbal problem solving are substantially hampered.

McVey et al (2016) emphasize that for children with ASD and intellectual disability, social competence development presents the most challenge. Lower intelligence is also identified to lower adaptive function in children with ASD and intellectual disability (McVey et al., 2016). Additionally, differences in IQ can contribute to ADHD variations in children with ASD (McVey et al., 2016). However, McClain et al. (2017) explain that autism severity may not be the best indicator of the severity of attention deficit and impulsive behaviour. Additionally, because of their low IQs, children with ASD may not do well in the long run. Consequently, as identified by Mazurek & Petroski (2015), only around 25% of people with autism and average intelligence are self-sufficient; the remaining 75% remain with their families until late adulthood or later.

2.3.4 Studies on the Neurodevelopment in Comorbid SCD and ASD Children

NDDs among children are well documented and it is established that children who are burdened with one NDD are at risk of comorbid diagnoses (Aguwa et al., 2021).

McNeely et al. (2021) sought to better understand the relationship between SCD and ASD to describe the clinical presentation of SCD and ASD through chart reviews of information collected from the medical history of documented diagnoses of both SCD and ASD patients. The study found no occurrence of SCD and ASD comorbidity in any of the patients studied. This finding further reiterates the rarity of ASD and SCD comorbidity. The researchers

however concluded that ASD should be considered in the differential diagnosis of patients with SCD and NDD and may present with atypical features in this population.

Lance et al. (2021) investigated the co-occurrence, associated traits, and risk factors for neurodevelopmental problems in a cohort of children with SCD. Their study sought to examine children with SCD and NDD both collectively and for each NDD. In contrast to children with SCD who do not have NDDs, the researchers found that children with SCD and NDDs, including ASD, were more likely to have a history of multiple SCD-related problems. The researchers concluded that children with SCD and ASD have a higher likelihood of developing specific disease-related problems.

Aguwa et al.'s (2021) investigation into the low diagnosis of NDDs among children with SCD was prompted by the hypothesis that low rates of neurodevelopmental screening and surveillance, particularly in young children, are the cause of the risk of NDDs being lower than anticipated in children with SCD. Like the study by McNeely et al. (2021), a retrospective chart analysis using the clinic rosters of 276 patients collected from hospitals with a paediatric haematology clinic and a sickle cell neurodevelopmental clinic was conducted. The study found that children with SCD are being screened by their healthcare providers at a substantially lower rate than the clinical guidelines call for and this is despite their acknowledged heightened risk. The study concluded that it is crucial to prioritize screening and surveillance for neurodevelopmental dysfunction in children with SCD because this vulnerable population is at higher risk for neurological complications including stroke, silent cerebral infarction, and neurodevelopmental disorders (NDD) and autism spectrum disorder (ASD).

The literature on neurodevelopment in comorbid SCD and ASD children suggests that SCD comorbid ASD is rare. However, the literature also indicates that the low rates of

neurodevelopmental screening and surveillance in children are the cause of the low diagnosis of SCD and ASD comorbidity; particularly, it is observed that children with SCD are often not screened for ASD when they are screened for NDDs further resulting in low rates SCD and ASD comorbidity.

CHAPTER THREE

METHODOLOGY

3.1 Introduction

This chapter provides information concerning the methods that were adopted in undertaking this research as well as a justification for the use of these approaches. Specifically, the chapter describes the various stages of the research, which include the selection of participants, the data collection tools and process and the process of data analysis.

3.2 Study Location

The sample was primarily recruited through specialist clinics at the Greater Accra Regional Hospital, Ridge and 37 Military Hospital in Accra, Ghana, particularly the Sickle Cell and Autism clinics. Further, samples were recruited through specialist Sickle Cell Disease and Neuropaediatric/Paediatrics and Child Health clinics at the Korle-Bu Teaching Hospital, as well as specialized clinics, special schools, special needs centres, parent support organizations and relevant social media groups.

3.3 Study Design

A cross-sectional study design has been adopted over the prospective cohort design. This was chosen given the limited time available for recruiting study participants and the rare comorbidity between SCD and ASD (which is the focus of this study). Furthermore, as this is a pilot study, a cross-sectional study design is appropriate given the purpose of the study is to generate a hypothesis instead of hypothesis testing.

3.4 Inclusion Criteria

Children were eligible for inclusion if 1) they were between 2 and 6 years old, and 2) had a diagnosis of SCD only or ASD only or comorbid SCD and ASD or typically developing.

3.5 Exclusion Criteria

Children were excluded if their parents refused to take part in the study during the informed consent process and when their parents were unable to speak the English language. In other words, participants without basic (not necessarily advanced) proficiency in the English language were excluded.

3.6 Sample Size

A total of 65 preschool-age children, with 20 participants in each of the three study groups and five in the comorbid group matched for gender, date of birth, neonatal clinical, and family social risks if feasible. As this was a pilot study, a formal sample size calculation was not undertaken.

3.7 Sampling Method

This study used a convenience sampling method.

3.8 Instruments for Data Collection

Two standardized parent-rating questionnaires that are valid for the study population were used to assess child neurodevelopment. Further, brief family sociodemographic information was also collected.

First, the Ages & Stages Questionnaires®, Third Edition (ASQ®-3), one of the most widely used neurodevelopmental screeners worldwide was used to assess child neurodevelopment. This tool is valid for assessing a range of outcomes in children between the ages of 1 to 66 months. Specifically, the following domains are assessed: gross motor skills, fine motor skills, communication skills, problem-solving/cognition skills, and social/ personal interaction. Parents respond to a series of questions with yes, sometimes and not yet. It took about 15-30 minutes to complete. This tool has been previously used in the Ghanaian population (Bello et al., 2013).

Second, the Language Use Inventory was used to assess social communication outcomes. This tool is valid for children between the ages of 18 to 47 months. Parents are required to answer a series of questions covering a broad range of settings and it takes about 20 minutes to complete. This tool is a recommended instrument by the NIH's National Institute on Deafness and Other Communication Disorders for pragmatics assessment while evaluating the efficacy of interventions targeting language acquisition in children with ASD. Furthermore, it is a recommended tool for Best Start's OnTrack Guide for Screening Tools in Ontario, Canada.

3.9 Data Collection/Procedure

Data collection involved a two-stage interview process:

1) informed consent; 2) standardized rating scale and questionnaire administration.

First, participants were contacted via phone call and provided with a detailed overview of the study procedures and invited to take part in the current study. They were informed that there were no expected direct benefits for the participants involved in this study; however, the results from this study may help better understand the impact of SCD and/or ASD on child development, which may help to improve future outcomes. They were assured that their and their ward's privacy will be always protected securely. Further, they were informed that participation in this research is voluntary. Carers who agreed to participate in the research study were asked to indicate their consent. This information was recorded by the researcher in the consent form with the date, time and full name and address of the participant. Please refer to Appendix 1 for the information sheet. Following the recording of informed consent (see Appendix 2), participants were administered the rating scales and questionnaires in an interview format by the researcher. Once the study was complete, to acknowledge their contributions, participants were provided with a small token of appreciation to compensate for their time.

3.10 Ethical Considerations

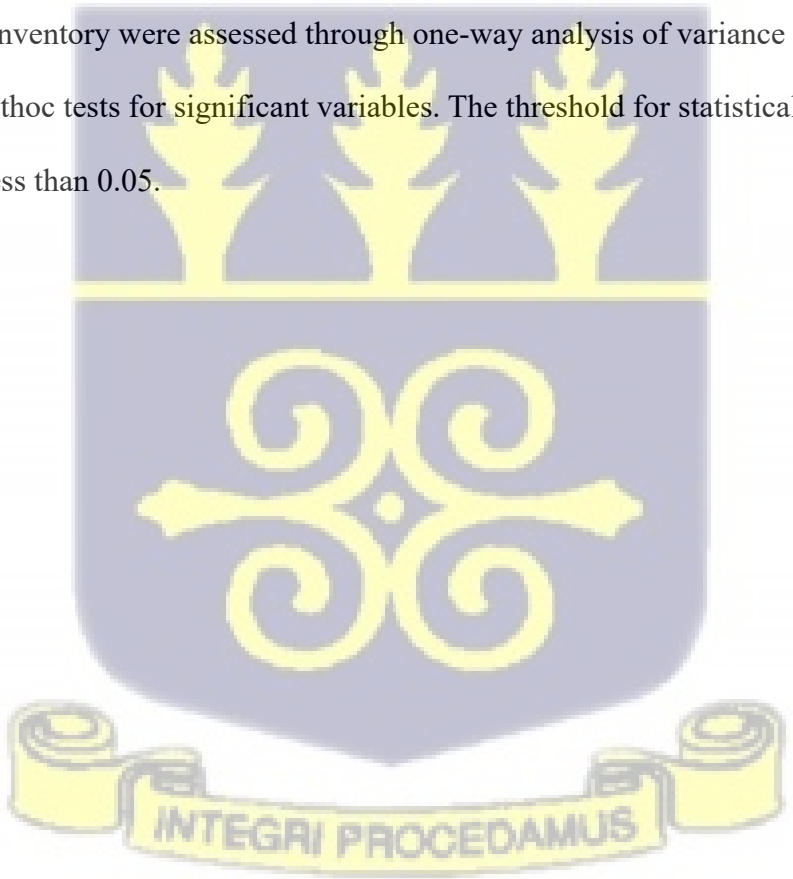
The study protocol was approved by the University of Ghana Ethics and Protocol Review Committee of the School of Biomedical and Allied Health Sciences (Ethics Identification Number: SBAHS/AA/ASLT/10700610/2021-2022). Ethical clearance was also sought from the various hospitals involved in the recruitment of study participants.

3.11 Data Control

The data collected were kept confidential by the researcher. Unique Identification Numbers were given to participants to keep them anonymous. Any hard-copy data files were stored in locked filing cabinets. Computers, external hard drives, and databases storing clinical and research data were password protected.

3.12 Data Analysis

IBM® SPSS Software Version 29.0 was used for data analysis. First, between-group comparisons of sample characteristics were undertaken using the Chi-squared test of independence. Second, between-group comparisons of scores on the ASQ®-3 domains and Language Use Inventory were assessed through one-way analysis of variance (ANOVA) followed by posthoc tests for significant variables. The threshold for statistical significance was a p-value less than 0.05.



CHAPTER 4

RESULTS

4.1 Introduction

This chapter is dedicated to the analysis of the findings obtained from the field. Due to the nature and objectives of the study, data obtained were analysed quantitatively using Excel and SPSS where results were presented in Table formats.

4.2 Demographic Data

This section investigates the demographic characteristics of the participants. The demographic data considered include the child's gender, hearing and vision challenges, and maternal sociodemographic data such as region of residence, marital status, ethnicity and educational qualifications.

As shown in Table 4.1, most of the children in the autism, as well as autism and SCD groups, were male, representing 75% and 80% respectively. Investigation into the sociodemographic data of the mothers of the participants also revealed that a minority were single or unmarried and this cut across all the various categories. Most of the parents included in this study were from the Greater Accra region of Ghana as shown across the various categories. With regards to ethnicity, most of the parents were Akans followed by the Ewe and Ga ethnic groups respectively. Finally, regarding educational qualifications, it was found that the majority of the parents of these children had attained higher education as their highest educational qualification. As shown in Table 4.1, no significant baseline differences were evident across the four study groups for gender ($p=.11$), hearing impairments ($p=.91$), vision impairments ($p=.73$) as well as maternal sociodemographic characteristics ($p>.05$).

Table 4. 1: Demographic Data of Participants

Characteristics, % (*n*)	**Typically Developing [*N*=20]**	**Sickle Cell Disease [*N*=20]**	**Autism [*N*=20]**	**Sickle Cell Disease & Autism [*N*=5]**	***p***
Child Clinical					
Male sex	45% (9)	45% (9)	75% (15)	80% (4)	.11
Hearing problems	5% (1)	10% (2)	10% (2)	0% (0)	.91
Vision problems	50% (10)	55% (11)	53% (10)	80% (4)	.73
Maternal Sociodemographic					
Single/unmarried	10% (2)	5% (1)	15% (3)	0% (0)	.79
Region of residence					
Central	0.0% (0)	5.0% (1)	0.0% (0)	0.0% (0)	
Greater Accra	90.0% (18)	90.0% (18)	80.0% (16)	100.0% (5)	
Volta	5.0% (1)	5.0% (1)	10.0% (2)	0.0% (0)	
Eastern	5.0% (1)	0.0% (0)	10.0% (2)	0.0% (0)	.85
Ethnicity					
Akan	55.0% (11)	55.0% (11)	65.0% (13)	40.0% (2)	
Ga/Dangame	15.0% (3)	5.0% (1)	0.0% (0)	20.0% (1)	

Characteristics, % (*n*)	**Typically Developing [*N*=20]**	**Sickle Cell Disease [*N*=20]**	**Autism [*N*=20]**	**Sickle Cell Disease & Autism [*N*=5]**	***p***
Ewe	20.0% (4)	40.0% (8)	25.0% (5)	40.0% (2)	
Guan	0.0% (0)	0.0% (0)	5.0% (1)	0.0% (0)	.52
Highest level of school					
Primary	0 (0.0%)	1 (5.0%)	0(0.0%)	0.0% (0)	
JSS/JSH	15.0% (3)	10.0% (2)	0.0% (0)	0.0% (0)	
SSS/SHS	5.0% (1)	5.0% (1)	25.0% (5)	0.0% (0)	
Secondary	0.0% (0)	0.0% (2)	0.0% (0)	0.0% (0)	
Higher	80.0%) (16)	70.0% (14)	75.0% (15)	100.0% (15)	.17

4.3 Performance on ASQ®-3 Domains

This study sought to investigate the performance of children across the four study groups on the ASQ®-3 domains. To achieve this, mean with standard deviation scores were recorded as shown in Table 4.2 below. As shown, with regards to communication, those in the typically developing and SCD categories recorded a mean score of 46.0 and 46.25 respectively with standard deviations of 15.78 and 14.32 respectively. However, those in the Autism and comorbid SCD & Autism category scored a rather lower mean of 6.0 and 20.0 respectively with standard deviations of 8.52 and 21.21. Furthermore, the findings also showed that with regards to Personal-Social, participants in the Typically Developing and SCD again scored much higher than those in the other two groups. As observed, they scored 47.50 with standard

deviations of 15.08 and 13.02 respectively as compared to participants in the Autism and SCD & Autism group who scored 22.63 and 18.0 with standard deviations of 13.02 respectively. Further investigation to establish the association between the various categories against communication revealed a significant association with $p<0.05$. However, there was no significant association between the various categories and Personal-Social skills.

The findings again revealed that despite the typically developing and SCD categories scoring higher means on the fine motor and problem-solving skills as compared to participants in the Autism and SCD & Autism categories, their level of association with the various skills did not show any significant association. This assertion was supported by $p>0.05$ for both the Fine Motor and Problem-Solving skills.

Based on the findings, conclusions can be drawn that there were no significant differences in the mean scores of any of the ASQ®-3 domains ($p>.05$) for children with comorbid SCD and autism compared with autism alone. However, children with comorbid SCD and autism had significantly lower scores on communication ($p<.001$), problem solving ($p=.008$), and personal-social ($p<.001$) domains than children with SCD only.

Table 4. 2: Performance on ASQ-3 Domains

ASQ-3 Domain Score, Mean (Standard Deviation)	Typically Developing [N=20]	Sickle Cell Disease [N=20]	Autism [N=20]	Sickle Cell Disease & Autism [N=5]	*p*			
					Overall	Sickle Cell Disease & Autism vs.		
						Typically Developing	Sickle Cell Disease	Autism
Communication	46.0 (15.78)	46.25 (14.32)	6.0 (8.52)	20.0 (21.21)	<.001	<.001	<.001	.049
Gross Motor	52.0 (6.57)	55.25 (9.67)	45.53 (14.2)	49.00 (12.45)	.046	.58	.25	.52
Fine Motor	44.75 (13.02)	42.0 (14.18)	15.53 (15.44)	29.0 (21.7)	<.001	.04	.09	.08
Problem Solving	47.25 (13.90)	49.0 (11.54)	22.89 (16.61)	28.0 (25.89)	<.001	.01	.008	.51
Personal-Social	47.50 (15.08)	47.50 (13.02)	22.63 (13.02)	18.0 (13.02)	<.001	<.001	<.001	.49

4.4 Performance on LUI Domains

This section investigates the performance of the participants on the Language Use Inventory (LUI) domains. Table 4.3 shows a summary of their average scores with their standard deviations across the four groups.

As observed in Table 4.3, in terms of social communication, while the comorbid and non-comorbid groups did not differ significantly in their usage of gestures ($p>.05$), there was a significant between-group difference for their word usage ($p<.05$), Further, children with comorbid SCD and autism had significantly lower scores on their usage of longer sentences than children with SCD only ($p=.002$).

Table 4. 3 :Performance on LUI Domains.

LUI Domain Score, Mean (Standard Deviation)	Typically Developing [N=20]	Sickle Cell Disease [N=20]	Autism [N=20]	Sickle Cell Disease & Autism [N=5]	*p*			
					Overall	Sickle Cell Disease & Autism vs.		
						Typically Developing	Sickle Cell Disease	Autism
Gestures	9.47 (4.64)	9.47 (4.00)	10.15 (2.64)	14.80 (12.43)	.93	.78	.78	.94
Words	24.05 (6.79)	22.68 (7.50)	6.32 (6.0)	14.80 (12.43)	<.001	.01	.04	.02
Longer sentences	89.16 (33.85)	78.70 (39.87)	10.70 (18.40)	27.80 (26.85)	<.001	<.001	.002	.28

CHAPTER 5

DISCUSSION

5.1 Introduction

This chapter presents the findings and discussions based on this pilot study aimed at examining preschool-age neurodevelopment, particularly early language outcomes of children with a comorbid diagnosis of SCD and ASD, relative to children with a diagnosis of SCD only, ASD only, and children with typical development. Participants were sought from specialist clinics at the Greater Accra Regional Hospital, the Korle-Bu Teaching Hospital and the 37 Military Hospital as well as other relevant sources including the use of social media. To achieve the objectives of the study, the researcher employed a cross-sectional, quantitative design using a convenience sampling technique. Parents of preschool children had their sociodemographic information collected as soon as they gave consent and were later interviewed over the phone using two standardised and culturally appropriate tools namely the Ages and Stages Questionnaire, 3rd edition and the Language Use Inventory. Within the study sample, there were no significant baseline differences evident between the four study groups for gender, hearing impairments, vision impairments, as well as maternal sociodemographic characteristics.

5.2 Performance on ASQ-3 Domains

The current study found no statistically significant differences in the mean scores of any of the ASQ®-3 domains for children with comorbid SCD and autism compared with autism alone. However, children with comorbid SCD and ASD had significantly lower scores on communication, problem solving, and personal-social domains than children with SCD only.

Findings align with McNeely et al. (2021) and Topal et al. (2018). It is likely that pre-school age children having trouble with their communication may find it challenging to express their needs and wants either verbally or non-verbally. These challenges could be as a result of communication barriers or obstacles which prevent the child from being exposed to an environment rich with language and also the acquisition and usage of non-verbal skills such as the use of gestures in communication. These communication barriers could result from a lack of knowledge on the part of the caregiver(s) either consciously or unconsciously regarding practises that will boost the child's communication skills there further deepening the slow rate of development for a child with either ASD or SCD comorbid SCD.

5.3 Performance on LUI Domains

In terms of social communication, while the comorbid and non-comorbid groups did not differ significantly in their usage of gestures, there was a significant between-group difference in their word usage. Further, children with comorbid SCD and ASD had significantly lower scores on their usage of longer sentences than children with SCD only. This affirms the finding in Swineford et.al, (2014) study that children with SCD and other conditions have reduced vocabulary and limited sentence structure. This could be attributed to other findings during the study where carers of the comorbidity group admitted to paying more attention to finding solutions to the effects of SCD symptoms which in some cases could be severe/debilitating on the child's general health and well-being thereby shifting their focus from language deficits and other challenges associated with ASD. Hence, they didn't seek intervention/ early intervention for their children.

5.4 Recommendations for Future Research:

1. It is recommended that a larger number of participants in the comorbid SCD and ASD group be prioritised. Although this is a rare comorbid pattern, the increased sample size is critical to enhancing statistical power and for robust conclusions.

2. During the process of participant selection, the researcher observed that most of the parents and/or carers were oblivious to the SCD genotype of their wards. The researcher, therefore, recommends that healthcare professionals should promote the significance of knowing their child's genotype to parents who visit the paediatric clinic and other specialist clinics.

3. Paediatric Doctors, Speech and Language Therapists and other healthcare professionals should be encouraged to upgrade their knowledge on children with comorbid SCD and autism and refer children with SCD who may exhibit autism red flags for further assessment.

5.5 Limitations of the Current Study

1. Owing to time constraints, the researcher was unable to conduct the study with as many participants as originally anticipated resulting in a relatively small sample size thereby limiting statistical power.

2. Poor record-keeping practices at some hospitals hampered the researchers' efforts to access the needed participants as some hospitals recorded all cases under the broad term of Neurodevelopmental Disorder without categorizing or labelling their records with a particular condition and/or comorbidity and the genotype of the child.

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APPENDIX 1: INFORMATION SHEET

Title of Research Project: Neurodevelopmental Outcomes of Preschool-Age Children with Sickle Cell Disease and Comorbid Autism Spectrum Disorder

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General Information about Research: The objective of this research project is to compare preschool-age neurodevelopment, particularly early language outcomes of children with a diagnosis of sickle cell disease and comorbid autism spectrum disorder, relative to children with a diagnosis of sickle cell disease only, autism spectrum disorder only, and children with typical development. You have been contacted as the parent/caregiver of a child between 2.5 and 6 years old and either typically developing or has a diagnosis of sickle cell disease only, autism only, or sickle cell disease with comorbid autism.

Voluntary Participation: If you do not wish to take part, you do not have to. If you consent to participate, you will be required to respond to a series of questions about your child's development and provide basic family sociodemographic information. This will take approximately 30 minutes.

Possible Risks and Benefits: There is no foreseeable risk of discomfort or harm because of participating in this research project. The only foreseeable burden may be an inconvenience (i.e., time to participate in research). There are no expected direct benefits for the participants involved in this research project; however, the results from this research may help better understand the impact of sickle cell disease and/or autism on child development.

Confidentiality: Please be assured that your and your child's confidentiality will be always protected securely. No personally identifiable information will be released to any third party at any time without your permission.

Compensation: Once you have completed all the questionnaires, to acknowledge your contributions, you will be provided with a small token of appreciation valued at less than 10 Ghanaian Cedi.

Contacts for Additional Information: For further information concerning the research, please contact the Ethical and Protocol Review Committee [EPRC] of the College of Health Sciences, University of Ghana. If you have any questions about your rights as a research participant you can contact the EPRC Office between the hours of 8 am and 5 pm on +233 [030] 294 0528, +233 [030] 266 5103, or email address: eprc@chs.edu.gh

For any other information, please contact Ms. Caroline Edwina Asiedu Okyere at xxxxxxxxxxx (email: xxxxxxxxxxx@gmail.com) or A/Prof Samudragupta Bora at xxxxxxxxx@mater.uq.edu.au

APPENDIX 2: RECORD OF INFORMED CONSENT

Record of Statement of Consent/Voluntary Agreement

- The purpose, benefits, risks, and procedures for the research, Neurodevelopmental Outcomes of Preschool-Age Children with Sickle Cell Disease and Comorbid Autism Spectrum Disorder, have been explained to the participant in detail in the language of their understanding.
- They were allowed to ask any question(s) about the research project and their question(s) has/have been answered to their satisfaction.
- They have been told that they may contact Ms. Caroline Edwina Asiedu Okyere at xxxxxxxxx (email: xxxxxxxxxx@gmail.com) or A/Prof Samudragupta Bora at xxxxxxxxxxxxxx@mater.uq.edu.au if they have questions about their rights as a study participant, to discuss problems and concerns or suggestions related to the research.
- It is implied that the participant named below agrees to participate in this research project voluntarily by completing the questionnaires and continuing with this study.

_____ _____

Name of Participant Date

_____ _____

Name and Signature of Researcher Obtaining Consent Date

Statement of Witness

I was present while the benefits, risks, and procedures were discussed with the participant. All questions were answered, and the participant agreed to take part in the research voluntarily.

_____ _____

Name and Signature of Witness Date