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ORIGINAL ARTICLE

Early-onset developmental impairments among infants attending the routine immunization clinic at the University College Hospital, Ibadan, Nigeria

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Developmental disorders are frequently overlooked in the developing countries, particularly in sub-Saharan Africa. Early identification of developmental delays (DDs) is critical to optimal outcomes. This study set out to determine the proportion of children who are at risk of DDs among infants attending immunization clinics at the University College Hospital, Ibadan, Nigeria. Infants 6 weeks to 12 months of age (median age 6 months) who presented for routine immunization were screened for DDs using the Ages and Stages Questionnaire. A total of 587 infants [312 (53.2%) males] were enrolled. A total of 198 (33.7%) children showed signs of DDs. For the domains of communication skills, fine motor skills, gross motor skills, problem solving/cognition skills and personal/social skills, the prevalences of DDs were 7.5%, 15.0%, 10.7%, 14.1% and 14.8%, respectively, and 14.3% had global DDs. Factors that significantly predicted DDs included prematurity (odds ratio [OR] 2.64 [95% confidence interval {CI} 1.45 to 2.05]) and a history of perinatal asphyxia (OR 1.74 [95% CI 1.77 to 2.49]). There is a need to incorporate routine developmental screening into the Nigerian healthcare system for timely recognition of DDs and prompt interventions.

Keywords: delay, development, infant, risk, screening, sub-Saharan Africa.

Introduction

Sub-Saharan African countries have witnessed some reduction in mortality rates in children <5 y of age, from 182 deaths/1000 births in 1990 to 78 deaths/1000 births in 2018.[1] Although, the region still accounted for 54% of the global deaths in children <5 y of age in 2018, many children who would have previously died as a result of complications during birth now survive, with many of these survivors experiencing developmental delays (DDs) and other health-related problems later in life. In addition, there has been a reduction in the mortality rates for conditions such as human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) among children in Africa and other developing parts of the world, with some of the survivors often experiencing DDs.[2] This brings a new challenge to the fore: how to recognise and meet the health needs of children with DDs/disabilities.

DDs occur when a child does not reach important developmental milestones within an expected period of time. About 250 million children <5 y of age in low- and middle-income countries (LMICs) are at risk of poor development.[3] This estimate is based solely on children thought to be at risk of poor development because of stunting or extreme poverty and does not take into account other risks for poor development that are not necessarily associated with poverty and stunting, such as maternal depression, violence against children, adverse environmental conditions and low maternal education.[4,5]

Early identification of DDs and institution of prompt interventions have been shown to significantly improve outcomes in affected children. Guevara et al.[6] randomised 2103 American children into either developmental screening using the Ages and Stages Questionnaire (ASQ) and the Modified Checklist for Autism in Toddlers or developmental surveillance and found that children who participated in the developmental screening program were more likely to be identified with DDs, referred to early intervention and were eligible for early intervention services in a timelier fashion than those on the surveillance program. Many high-income countries have programs in place for early identification of children with DDs and referral for appropriate interventions. Unfortunately, the majority of LMICs lack well-established programmes for routine developmental screening in children. This is

a major reason for the lack of epidemiological data and unavailability of appropriate interventions for children with DDs in these countries.[7]

The lack of epidemiological data leaves a huge gap in planning services for individuals with DDs in Nigeria and other parts of sub-Saharan Africa. Healthcare programs for children in LMICs are largely limited to physical growth monitoring and management of acute illnesses, with little attention towards developmental monitoring for prompt identification of infants and young children with DDs who would benefit from early interventions. Unfortunately this window of opportunity that presents in the first year of life is often missed. Therefore our study focused on children between birth and 12 months. We performed developmental screening in infants attending the routine infant immunization clinic at the University College Hospital, Ibadan, Nigeria, using the ASQ-3 to determine the proportion of children who might be at risk of DDs and the correlates of DDs. We anticipated that this study would provide valuable information for defining the magnitude of the problem, identifying the risk factors for DDs and provide baseline justification of the need for the inclusion of routine developmental screening services as part of routine infant welfare services in Nigeria. We hope this will also serve as a template for other resource-poor countries in Africa.

Methods

Participants

Participants in this study were mothers and infants attending the routine immunization clinic of the University College Hospital, Ibadan, Nigeria recruited through a sample of convenience method if they met the following inclusion criteria: interviewee was the mother and the infant was 6 weeks to 12 months of age, had no symptoms or signs of acute illness at the time of screening and had not been previously diagnosed with a neurodevelopmental disorder (NDD). Children who were brought to the clinic by a person other than the mother or whose mother refused to give written consent were excluded from the study.

The formula below was used for estimation of the sample size:

$$n = \frac{Z^2pq}{d^2},$$

where n=minimum sample size, Z=1.96 (the standard normal deviate for the required confidence level of 95%), α=5%, p=prevalence of developmental disability (assuming a figure of 50%), q=1−p and d=margin of error (0.045). Thus

$$n = \frac{(1.96)^2 \times 0.5 \times (1 - -0.5)}{(0.045)^2} = 474.$$

Assuming a non-response rate of 15%, the minimum sample size would be 474+(15%×474)=474+71=545.

Study instrument

The ASQ-3 was used to screen the children in this study.[8] The tool is applicable as a researcher-administered and self-administered assessment form. It is composed of 21 sets of questions covering an age range of 2–60 months. The questionnaire covers the five key developmental areas: gross motor skills, fine motor skills, communication skills, problem solving/cognition skills and personal/social skills. Each set is composed of 30 items, 6 in each domain. Responses to items in all the domains are scored as follows: 'yes' (10 points), 'sometimes' (5 points) and 'not yet' (0 points).[8] The maximum score in each domain is 60 points. Scores obtained from each domain are compared with established cut-off points at 1 and 2 standard deviations (SDs) that are used to identify children at risk of DDs. If the score on any domain falls below the 2 SD cut-off, referral for further assessment is advised. If the score on any domain is within the 1–2 SD cut-off point, it is advised to provide learning activities and monitor the child's development. The ASQ has been proven to be reliable in detecting DDs in children <5 y of age. One study reported an adjusted sensitivity and specificity of 87.4% (95% confidence interval [CI] 62.9 to 96.6) and 82.3% (95% CI 80.5 to 83.9), respectively.[9] It was also reported to be valid among children from low-income families.[10]

Study procedure

The study was approved by the University of Ibadan/University College Hospital Ethical Review Committee. Clear information regarding the study procedure was provided to the caregivers in their preferred language, after which caregivers of the participants signed a written informed consent. Demographic and other clinical characteristics of the participants such as age, gestational age at birth, history suggestive of any adverse perinatal and neonatal events (e.g. perinatal asphyxia, sepsis, neonatal jaundice and neonatal seizures) were obtained from the caregiver. The age-appropriate ASQ-3 was then administered to the caregiver. The items on the questionnaire were explained to the participants where necessary. The total scores were calculated based on the caregivers' responses and plotted on the scoring guide to categorise each child's development into one of three categories: development progressing on schedule, requires further monitoring (borderline) or at risk of developmental delay. Infants who failed in two or more domains of development were classified as being at risk of global DD, defined as a delay in two or more developmental domains of gross/fine motor skills, speech/language, cognition, personal/social skills and activities of daily living affecting children <5 y of age.[11]

Data analysis

Data were analysed using the Statistical Package for Social Science version 20 (IBM, Armonk, NY). A summary of the data was presented using simple percentages and frequency. The associations between DDs and the selected risk factors, i.e. a history of perinatal asphyxia, neonatal jaundice and prematurity, were determined using the χ^2 test. The level of significance was set at $p<0.05$.

Results

Characteristics of the participants

Participants in this study were 587 mother–infant pairs. The ages of the infants ranged from 6 weeks to 12 months, with a median age of 6 months. Table 1 shows the characteristics of the infants.

Table 1. Characteristics of the 587 infants studied

Characteristics	Values
Gender, n (%)	
Male	312 (53.2)
Female	275 (46.8)
Age	
Mean	7.6±4.1 months
Median	6 months
Range	6 weeks–12 months
Gestational age at birth, n (%)	
Preterm (<37 weeks)	151 (25.7)
Term (37–40 weeks)	436 (74.3)
History suggestive of perinatal asphyxia, n (%)	
Yes	54 (7.8)
No	533 (92.2)
History of neonatal jaundice, n (%)	
Yes	156 (22.6)
No	431 (77.4)
More than one risk factor, n (%)	
Yes	38 (6.5)
No	549 (93.5)

A total of 312 (53.2%) were males and 151 (25.7%) were born before 37 weeks of gestation. There was positive history of neonatal jaundice in 156 (22.6%) and 54 (7.8%) reported a history suggestive of perinatal asphyxia. Thirty-eight (6.5%) of the infants had at least two of the risk factors for DDs, i.e. prematurity, neonatal jaundice and perinatal asphyxia.

Prevalence of DDs

Table 2 shows the outcomes of developmental screening by the ASQ-3 in the 587 infants. A total of 198 (33.7%) children showed signs of DDs in at least one of the five domains assessed. For the domains of communication, fine motor skills, gross motor skills, problem solving and personal/social skills, the prevalences of DDs were 7.5%, 15.0%, 10.7%, 14.1% and 14.8%, respectively. Eighty-four (14.3%) children failed in two or more domains of development and were noted to be at risk of global DDs.

Relationship between characteristics of the infants and performance across the five developmental domains as tested by the ASQ-3

Table 3 shows the relationship between the characteristics of the participants and the performance across the five developmental domains. There was a significant association between gestational age at birth and performance in the communication domain (χ^2=16.238; p=0.003), the gross motor skills domain (χ^2=15.867; p<0.001) and the fine motor skills domain (χ^2=29.036; p<0.001). The association between gestational age at birth and the problem-solving domain of development (χ^2=24.169; p<0.001) and the personal/social domain (χ^2=17.138; p=0.001) were equally significant.

There was also a statistically significant association between history of birth asphyxia and the risk of delay in the communication (χ^2=14.665; p=0.002), fine motor skills (χ^2=31.673; p<0.001), gross motor skills (χ^2=25.065; p<0.001), problem-solving (χ^2=19.709; p<0.001) and personal/social (χ^2=9.430; p=0.009) domains. A history of jaundice was significantly associated with a risk of delay in the problem-solving domain (χ^2=10.832; p=0.013). There was a statistically significant association (p<0.001) between having more than one risk factor and delay in all the domains of development. No significant association was found between gender and performance in the developmental domains.

Discussion

One-third of the children who were screened in our study were found to be at risk of DDs in at least one of the five domains of development. Prevalence studies on DDs have reported divergent figures ranging from 6.4 to 44.3%.[12–14] A study that was conducted in Ghana, a country that shares a border with Nigeria, reported that 44.3% of the children who were screened had DDs in the different domains of the ASQ.[12] The disparity in the prevalence of DDs reported in the two studies might have been due to differences in the ages of the participants enrolled in the studies and differences in the settings of the study locations. While our study assessed infants between the ages of 6 weeks and 12 months, the Ghana study assessed children from birth to 5 y. In addition, our study was carried out in a metropolitan city while the Ghana study was done in a rural setting, which may account for the higher prevalence of DDs reported in that study.

Another study that used the Neuropediatric Development (NPED) screening tool for NDDs among 400 children ages 1–60 months in four communities in Mexico and Cuba found an overall prevalence of 21.5%.[15] The prevalence reported in that study was much lower than what we found and might be related to the fact that the instruments used for developmental screening were different. In Peru, 593 children between the ages of 8 and 39 months were screened with the ASQ. The authors reported a prevalence of 26.7% for DDs in the Amazonian communities.[14] Although our study and the Peru study share some similarities in terms of the sample size and the use of the ASQ as the screening tool, we found a higher prevalence of DDs in Nigerian infants.

In contrast, other studies have reported much lower prevalences of DDs in their cohorts. In India, Sachdeva et al.[16] assessed 478 children <3 y of age and found a prevalence of 7.1% for global DD. Demirci and Kartal,[13] in a cross-sectional, descriptive study involving 1514 Turkish children ages 3–60 months assessed by the ASQ, reported a prevalence of 6.4% for global DD, which is significantly lower than the 14.3% we found in our study. This might be related to the influence of socio-economic status on child development. Children in Turkey, a country classified as an upper-middle-income country, are more likely to fare better with regards to development than their counterparts in LMICs. A sample of 694 children who were 3 y of age in the United Arab Emirates were evaluated on the Denver Developmental Screening Test and 8.4% of them tested positive for developmental disorder.[17] The discrepancies in the findings from the different studies can be attributed to variations in the geographical locations

Table 2. Outcome of developmental screening by the ASQ-3 across the five domains in 587 infants

Domain	Development on schedule, n (%)	Borderline, n (%)	Delayed, n (%)
Communication	447 (76.1)	96 (16.4)	44 (7.5)
Fine motor skills	425 (72.4)	74 (12.6)	88 (15.0)
Gross motor skills	440 (75.0)	84 (14.3)	63 (10.7)
Problem solving	400 (68.1)	104 (17.7)	83 (14.1)
Personal/social skills	432 (73.6)	68 (11.6)	87 (14.8)

Table 3. Relationship between characteristics of the infants and performance across the five developmental domains of ASQ-3

	Communication		Gross motor skills		Fine motor skills		Problem solving		Personal/social skills	
Factor	χ^2	p-Value	χ^2	p-Value	χ^2	p-Value	χ^2	p-Value	χ^2	p-Value
Gender	6.821	0.146	5.160	0.164	1.751	0.626	2.704	0.439	3.335	0.343
Gestational age	16.238	**0.003**	15.867	**0.001**	29.039	**<0.001**	24.169	**<0.001**	17.138	**0.001**
Birth asphyxia	14.665	**0.002**	31.673	**<0.001**	25.065	**<0.001**	19.709	**<0.001**	9.430	**0.009**
History of neonatal jaundice	3.323	0.505	4.347	0.206	4.171	0.244	10.832	**0.013**	7.428	0.059
More than one risk factor	26.345	**<0.001**	24.732	**<0.001**	34.531	**<0.001**	20.932	**<0.001**	31.543	<0.001

Significant values ($p<0.05$) are in bold.
[a]Presence of more than one risk factor of prematurity at birth, birth asphyxia and neonatal jaundice.

of the study sites, the use of different developmental assessment tools and variations in the age of study participants and case definitions and criteria for DDs. The higher prevalences for DDs are largely from LMICs.

It has been reported that causes of DDs are abundant in LMICs. In 2007 a Lancet series looked at developmental issues in developing countries and reported that >200 million children <5 y of age in LMICs will fail to reach their developmental potential.[18] The factors attributed to this failure were stunting and extreme poverty. The Global Burden of Disease Study 2016 provided a comprehensive assessment of prevalence and years lost to disabilities for developmental disabilities among children <5 y of age in 195 countries from 1990 to 2016. The study showed that the global burden of developmental disabilities has not significantly improved since 1990, suggesting inadequate global attention on the developmental potential of children who survive childhood as a result of child survival programmes, particularly in sub-Saharan Africa and South Asia.[19] More recent estimates have shown that at least 250 million children in LMICs are at risk of DDs.[3] It is therefore imperative to focus the required attention on timely recognition and early diagnosis of DDs for prompt intervention, particularly in LMICs.

Studies have linked socio-economic factors to brain development, with more studies finding an association between poor development and lower socioeconomic status.[20,21] For example, children from lower socio-economic classes tend to develop language later.[22] The maternal level of education has been linked to chid development, with children born to mothers without formal education (defined in most cases as a minimum of 6 y of formal education) being at an increased risk of experiencing DDs.[23,24] Other factors that have been found to be associated with developmental disorders include poverty, malnutrition and perinatal and neonatal complications.[19] Although many of these causes of DDs are well understood and preventable, established methods of prevention are not being fully implemented in developing countries, with most of the available resources being focused on other childhood diseases to the neglect of NDDs. Research efforts, including funding, are mostly directed towards vaccine-preventable childhood illnesses, bacterial and viral infections including HIV/AIDS, parasitic infestations, nutritional deficiencies and injuries, with very little attention towards NDDs.

Several other factors have also been reported to affect development in children. Prematurity, neonatal jaundice and birth asphyxia were found to be strongly associated with DDs in our study. These factors have been consistently documented to be associated with DDs through different mechanisms. Prematurity has been found to be associated with complications like intraventricular haemorrhage and this could well be responsible for developmental problems including cerebral palsy, especially the spastic diplegia type.[25] In addition, evidence from neuroscience shows that microstructural and neural connectivity processes are disturbed because of prematurity, and preterm birth perturbs the genetically determined programme of corticogenesis in the developing brain.[26] Our study showed that 25.7% of the infants were born prematurely, 7.8% had a history suggestive of perinatal asphyxia and 22.6% had neonatal jaundice. Further analysis showed that these factors were significantly associated with an increased risk of DDs in all five domains of the ASQ-3. A Norwegian

longitudinal sample of 1555 infants attending a well-baby clinic who were assessed with the ASQ found that a gestational age <37 weeks was significantly associated with a delay in the communication domain later in life.[27] In a community-based, stratified cohort study, parents of 832 moderately preterm children ages 43–49 months were asked to complete the ASQ. It was reported that children who had neonatal jaundice were 3 times more likely to have DDs during the preschool years.[25]

The study by Sachdeva et al.[16] noted that prematurity and a history of seizures were predictors of global DD. Similarly, Alwan et al.[28] found perinatal asphyxia and prematurity as major risk factors for DD in a cohort of 75 children ages 8 months to 5.5 y with global DD. Thomaidis et al.,[29] in a longitudinal study, assessed the effect of prenatal and perinatal risk factors on the severity and outcome of global DD in 142 children and reported that prematurity was significantly related to the severity of global DD. Our findings are thus consistent with previous reports.

LMICs are still far behind in surveillance, screening and monitoring efforts on early child development.[30,31] Identifying DDs in children early by a validated, reliable, parent-completed questionnaire like the ASQ and detecting risk factors for DDs are crucial for primary care. Our study has provided valuable information on the prevalence of DDs based on a standardised instrument for developmental screening and the factors associated with DDs in a cohort of Nigerian infants. We hope the information provided in our study will be useful for stakeholders to adequately plan the necessary assessment and intervention responses. Our study is also a step in the right direction by providing a clear picture for policymakers in developing countries to provide early identification and intervention services for children with DDs.

Conclusions

Our study showed that one of every three children presenting at our routine infant immunization clinic is at risk of DDs. Perinatal asphyxia and prematurity are major risk factors for DDs in our cohort. Early identification of DDs in infants and young children by a validated, reliable, parent-completed questionnaire and detection of risk factors for DDs are crucial for primary care.

Authors' contributions: YA and IL conceived and designed the study. YA, IL, AA, IO and AAO implemented the study. YA and IL wrote the first draft of the manuscript, AA, AAO and IO contributed significantly to improve the draft. All authors read and approved the final draft.

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