The Impact of Iron Status in Early Infancy on Neurodevelopment of Rural Gambian Infants.

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Background

One in three children in low- and middle-income countries fail to reach developmental milestones by school age [1].

These early deficits have been associated with poorer academic achievement, economic success, and mental health across the lifespan [2].

Iron deficiency effects a quarter of pre-school age children globally and is most prevalent in sub Saharan Africa [3].

Iron is involved in many processes of neurodevelopment including myelination, synaptogenesis, and dopaminergic neurotransmission. Therefore iron deficiency may contribute to neurodevelopmental faltering.

The first 1000 days (conception to 2 years of age) are a critical window for neurodevelopment. Despite this, a recent review concluded that there is insufficient research into early iron status (0-6months of age) and neurodevelopment particularly in sub Saharan Africa [4].

The aim of this study was to assess the relationship between iron status from 0-6 months of age and trajectories of neurodevelopment from 5-18 months of age, using the Mullen Scales of Early Learning (MSEL), a tool to assess infant development across language, motor and sensory domains, in a cohort of infants in rural Gambia.

Methods

Blood samples were collected from infants at 1 and 5 months of age, then analysed for the following markers of iron status; soluble transferrin receptor (sTFR), ferritin, and c-reactive protein (CRP) using a COBAS 6000 analyser.

The MSEL was conducted at 5, 8, 12 and 18 months of age, and total cognitive score was calculated at each time point.

Individual trajectories of development were modelled using mixed effects modelling. sTFR was entered as the main exposure, models were adjusted for sex, birth season, length, head circumference, parental education and socio-economic status.

Abstract

One in three children growing up in low-and-middle-income countries do not achieve expected developmental milestones by pre-school age.

Iron deficiency is the most common micronutrient deficiency globally and may be one contributing factor.

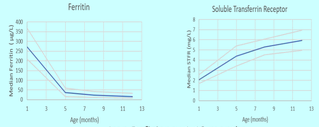
A recent review concluded that there is insufficient research into the impact of early iron status on neurodevelopment, particularly in sub Saharan Africa

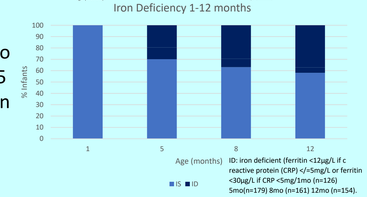
This study assessed the impact of iron status at 1 & 5 months of age on developmental trajectories from 5-18 months of age among a cohort in rural Gambia.

Findings showed that infants with poorer iron status at 5 months of age achieved lower scores at 5 months. The difference was not recovered by 18 months of age.

Results

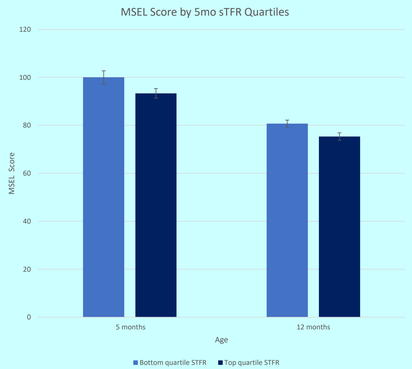
Infant iron status declined rapidly between 1-12 months of age. All infants were iron sufficient at 1month of age. However, 30% and 42% of infants were iron deficient by 5 and 12 months of age, respectively (ferritin <12µg/L or <30µg/L if CRP>5mg/L).





ID: iron deficient (ferritin <12µg/L if c reactive protein (CRP) </=5mg/L or ferritin <30µg/L if CRP <5mg/1mo (n=126) 5mo(n=179) 8mo (n=161) 12mo (n=154).

Iron status at 1 month of age was not associated with MSEL scores at any age (p>0.05). However, compared to infants in the top (poor iron status) quartile of sTFR at 5 months of age, infants in the bottom quartile (good iron status) scored 7(93.4 vs 100.1 p=0.048) and 5 points higher (75.4 vs 80.7 p=0.01) at 5 and 18 months of age respectively.



Observations=475 N= 147	Co-efficient (SE)	P Value
Constant	6.52 (0.15)	<0.001
Fixed Effects		
Age (months)*	2.56 (0.15)	<0.001
5-month sTFR (mg/L)	-0.57 (0.15)	<0.001
5-month sTFR * age	0.010 (0.02)	0.667
Random Effects		
Variance (Age*)	0.07 (0.02)	
Variance (Constant)	0.014 (0.01)	
Covariance (age, cons)	0.032 (0.01)	
Residual	14.76 (1.14)	

*** Age centred to 5 months. Model adjusted for predefined factors listed in methods.**

In a mixed effects model of individual developmental trajectories (5-18 months), a 1 SD increase in 5 month sTFR (1.6mg/L) was associated with a 0.2 SD (2.0 points) reduction in 5 month MSEL score , this difference in scores was maintained from 5-18 months (age*sTFR interaction p>0.05).

Conclusion

One third of infants were iron deficient by 5 months of age. Poorer iron status at 5 months, but not 1 month of age, was associated with lower MSEL scores at 5 months of age. This difference in scores was not recovered by 18 months of age. Future research should assess whether interventions to maintain iron status from 0-6 months are beneficial for neurodevelopment.

References: McCoy et al, 2016 Early Childhood Developmental Status in Low- and Middle-Income Countries: National, Regional, and Global Prevalence Estimates Using Predictive Modeling. PLOS Medicine 14(1). 2. Grantham McGregor et al 2007. Developmental potential in the first 5 years for children in developing countries. The Lancet 369 (9555). 3.Lozoff & Georgieff 2006. Iron Deficiency and Brain Development Pediatric Neurology 12 (3). 4. McCann et al 2020. The Role of Iron in Brain Development: A Systematic Review. Nutrients 12(7). **Acknowledgements: I would like to acknowledge the participants and staff of the BRIGHT project, and the BRIGHT project funders The Bill and Melinda Gates Foundation.**