Body composition during early infancy and mental health outcomes at 5 years of age: A prospective cohort study of Ethiopian children

Mubarek Abera[1,2*], Markos Tesfaye[3], Charlotte Hanlon[4,5], Bitiya Admassu[2,6], Tsinuel Girma[7], Jonathan C. Wells[8], Pernille Kæstel[2], Christian Ritz[2], Rasmus Wibaek[2,9], Kim F. Michaelsen[2], Henrik Friis[2], Gregers S. Andersen[9] P

Email: MA: mubarek.abera@ju.edu.et, abmubarek@gmail.com; MT: markos.tesfaye@sphmmc.edu.et; CH:charlotte.hanlon@kcl.ac.uk; TG: tsinuel@yahoo.com; JW: jonathan.wells@ucl.ac.uk; GA: gregers.stig.andersen@regionh.dk; CR: ritz@nexs.ku.dk; BA: bitiyaa@yahoo.com; RW: rasmus.wibaek.christensen@regionh.dk; KM: kfm@nexs.ku.dk; HF: hfr@nexs.ku.dk; PK: pernille.kaestel@gmail.com

Affiliation

[1]Department of Psychiatry, Faculty of Medical Sciences, Jimma University, Jimma, Ethiopia
[2]Department of Nutrition, Exercise and Sports, University of Copenhagen, Denmark
[3]Department of Psychiatry, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia
[4] Addis Ababa University, Department of Psychiatry, School of Medicine, College of Health Sciences, Addis Ababa, Ethiopia
[5] King's College London, Centre for Global Mental Health, Institute of Psychiatry, Psychology and Neuroscience, London, UK
[6]Department of Population and Family Health, Faculty of Public Health, Jimma University, Jimma, Ethiopia
[7]Department of Paediatrics and Child Health, College of Health Sciences, Jimma University, Jimma, Ethiopia
[8]Childhood Nutrition Research Centre UCL Institute of Child Health, London WC1N 1EH, UK
[9]Steno Diabetes Center Copenhagen, Gentofte, Denmark

[*]Corresponding author: Mubarek Abera, Department of Psychiatry, Faculty of Medical Sciences, Jimma University, Ethiopia, PO Box 378, Jimma, Ethiopia. mubarek.abera@ju.edu.et; abmubarek@gmail.com; Mob.phone:+251 913332483

Funding Source: Danish Council for Strategic Research—Program Commission on Food and Health; Danida through the Consultative Research Committee for Development Research (104. Dan.8-1207 and 09-097 LIFE). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript

Financial Disclosure: None
Conflict of Interest: None of the authors had declared conflicts of interest

Abstract

Objective: To examine the relationship between body composition, (specifically fat (FM) and fat-free mass (FFM) in early infancy), and mental health outcomes in early childhood.

Methods: In the infant anthropometry and body composition (iABC) birth cohort study from Ethiopia, body composition was measured at birth and 1.5, 2.5, 3.5 4.5 and 6 months of age**.** Mental health was assessed at 5 years of age using the approved Amharic version of the Strengths and Difficulties Questionnaire (SDQ), a parent report scale covering four different domains providing a total difficulties score. The associations of FM or FFM at birth as well as during early infancy, with SDQ score at 5 years of age were examined using multiple linear regression analyses.

Results: At five years of age, the mean (±SD) for SDQ score was 10.4 ± 5.8. FM at birth was positively and FFM negatively associated with SDQ score. For each kg increase in FM at birth, the SDQ score at 5 years was 5.7 points higher (β=5.7; 95% CI 1.4,10.0). In contrast, for each kg increase in FFM at birth, the SDQ score was 3.9 points lower (β=-3.9; 95% CI -7.0, -0.8). Neither FM nor FFM accretion rate during early infancy were associated with SDQ score at 5 years of age.

Conclusions: Fetal rather than infant body composition was associated with SDQ score at 5 years of age. Greater FFM accretion during fetal life may have contributed to more optimal neurobehavioral development during early life. However, the potential mechanisms underlying the observed associations need further investigation.

Key words

Introduction

The emotional and behavioural development of children is an important aspect of child health and wellbeing (1,2). Higher degree of emotional and behavioural problems (EBP) contribute to poorer mental health of children and adolescents (3). In a meta-analysis from sub-Saharan Africa, the magnitude of childhood mental health problems ranged from 2% - 27% (4) and a multi-centre study from low income countries reported the range to be from 12% - 29% (5). These childhood EBPs may persist and increase the risk of mental disorders in adult life (6,7). EBPs may impede a child's school engagement and academic attainment (8,9) and lead to poorer social skills, functioning, and economic status in adulthood (10).

Several overlapping risk factors have been shown to predict EBPs in preschool children (11–16). An interaction between social, environmental and biological factors typically contribute to childhood mental health problems (17), including poor parenting skills, child maltreatment, poverty, parental stress and mental illness, inadequate stimulation, poor adult role models and different adverse life experiences during early life (18–21). Genetic predisposition, neurobiological deficits, trauma to the brain, neurological diseases including those resulting from infections, fetal exposure to different toxins and substances, neurochemical disturbances, and not least, impaired fetal and infant nutrition and growth constitute potential biological risk factors (14,15,17,22). Specifically with regards to fetal and infant nutrition and growth, higher maternal body mass index (BMI) during pregnancy, fetal malnutrition, and both high or low birth weight have all been identified as risk factors for EBPs (22–24). However, no evidence has been reported on the mechanisms through which maternal BMI, and high or low birth weight may relate to EBPs. Some investigators have hypothesised that higher maternal weight gain during pregnancy could result in greater adiposity in the newborn (25,26) leading to increased EBPs among children (27). However, studies that found associations between newborn or infant weight and growth with EBPs relied on simple measures of anthropometric indices.

From the infant anthropometry and body composition (iABC) birth cohort (28,29), and other cohorts (30), it has been shown that there is significant variability in fat and lean mass within a given weight at birth or in infancy, which is not captured in simple anthropometric measures. Moreover, it is not known how this variability influences associations between early growth and mental health outcomes in childhood. In this study, we examined the differential relations of fat- and fat-free mass during fetal life and infancy with mental health status at 5 years of age.

Method and participants

The iABC birth cohort was established and followed during early infancy and at five years of age in Jimma, Ethiopia. A total of 644 mother-newborn pairs were recruited at delivery. Pairs were excluded from the study if the family lived outside Jimma town, gave birth to a preterm infant or an infant with congenital anomalies, or an infant with a birth weight of ≤ 1500g. Within 48 hours of delivery at the hospital, mothers and their newborn babies were examined for baseline information. Further details of the cohort and the setting have been published elsewhere (28,29,31,32).

Baseline measurement

FM, FFM, birth weight, length, and head circumference of the newborn were measured as described elsewhere (28). In short, FM and FFM were measured using a PEA POD® (COSMED, Rome, Italy), an air displacement plethysmography method (ADP), which is an accurate and reliable method of body composition (BC) assessment (28). Sex and birth order of the newborn were recorded. Maternal weight (kg) to the nearest 0.1kg and height to the nearest 0.1cm, were measured after delivery using a Tanita 418 (Tanita Corp. USA) scale and a

SECA214 stadiometer (SECA, Hamburg, Germany), respectively. As only a few mothers in the study area have an ultrasound scan performed, the new Ballard score assessment method (33) was used to estimate the gestational age of the newborn. Family wealth index (31), maternal age and parental education were assessed using a structured questionnaire.

Follow up measurements

During the follow up at 1.5, 2.5, 3.5, 4.5, and 6 months of age, FM, FFM, weight, and length of the infant were measured with the same approach used for the baseline measurement. The same parameters were measured again at 5 years of age. Childhood mental health status was assessed at 5 years of age using the Strengths and Difficulties Questionnaire (SDQ), parent version (3). The SDQ has 25 items categorized into five different subscales: four subscales contributing to a total difficulties (SDQ) score and a fifth subscale to identify strengths. Each item has a response category from 0-2: 0: not true, 1: somewhat true, and 2: certainly true. The SDQ subscales are emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems and the strengths scale (prosocial behaviour), each comprising five items with a maximum score of 10. It is further recommended that the SDQ groups the 4 difficulty-subscales into two major 'internalising' and 'externalising' scales, each with a maximum score of 20. The sum of conduct and hyperactivity subscales constitutes the externalising scale, while the sum of emotional symptoms and peer problems constitutes the internalising scale. Internalising problems are characterized by anxiety, depression, loneliness, poor self-esteem and suicidal behaviour. On the contrary, externalising problems are characterized by presence of aggression, restlessness, stealing, cheating and disobeying rules. The overall total difficulties score ranges from 0 – 40 and is computed by adding the scores for the four difficulties subscales. Higher scores on the SDQ scale are associated with greater risk of mental health problems (3,34). An authorised

Amharic version of the SDQ is available (35) and has shown good construct and convergent validity in the Ethiopian context (34). Using SDQ, the child's behaviour over the last six months before the date of interview was assessed.

Maternal mental health status at the 5-year follow up was assessed using the Kessler-6 (K-6) mental distress screening tool (36,37). The K-6 is a 6-item scale asking for the presence or absence of symptoms of mental distress during the last one month before the date of interview. It has a response options of; 0: never, 1: a little of the time, 2: some of the time, 3: most of the time, 4: all the time. K-6 has a score ranging from 0 (minimum) to 24 (maximum) mental distress score. The K-6 has also been validated in the Ethiopian context (37). Family structure at the 5-year follow up was collected by self-report.

Research staff training included a pilot test at the initiation of the study. Research staff met weekly to take corrective measures related to the data collection process. The peapod was calibrated daily, and ambient temperature was regulated. Only four clinical research nurses, all with significant research experience, were involved in collecting the SDQ data. Analyses were adjusted for data collector to control for any interpersonal variability between research nurses.

Ethical considerations

Ethical approval was obtained from the research review board of the College of Public Health and Medical Sciences, Jimma University (reference RPO/56/2001). Mothers were only enrolled in the study if they gave informed consent. Transportation costs were reimbursed. Mothers and children who needed medical attention were linked to the psychiatric or paediatric unit of Jimma University Specialized Hospital.

Data analysis

Data were double entered to Epidata 3.1 (The EpiData Association, Odense, Denmark) (38) and exported to STATA version 12.1 (Texas, USA) for cleaning and analysis. Categorical variables were described as frequencies and percentages, while continuous variables were described using the relevant indicators of central tendency and spread (mean and standard deviation (SD) or median and interquartile range (IQR)). Outliers, normality, and multi-collinearity were assessed. Using the lambda-mu-sigma (LMS) method to derive centile charts for birth to 6 months for FM and FFM growth, a linear growth pattern for 0-6 months was identified for FFM while a linear growth pattern for FM was identified for 0-4 months and 4-6 months of age, respectively (29). Thus, summary rates of FFM accretion for 0-6 months and of FM growth for 0-4 and 4-6 months of age were predicted using a linear mixed effects model. The method is described in detail elsewhere (39). For the outcome variable, the response ranging from 0-2 for each item assessing for difficulties were summed to obtain an aggregate total difficulty score ranging from 0 – 40. Those positively phrased items in the questionnaire were reverse coded during the analysis.

Linear regression models were used to evaluate the association between FM or FFM at birth and during early infancy (0-6 months) and SDQ score at 5 years of age. The estimate (β coefficient) and 95% CI were reported to describe the associations. Covariates were selected based on evidence from existing literature and presence of biologically plausible relationships between the covariates and the outcome variable. Covariates that change (affect) the estimate for the main exposure were included in the regression model.

Two sets of regression models were developed. The outcome variables for both sets of regression models were total difficulty (SDQ) score, internalising problem score, and externalising problem score. The first set of regression model contained FM or FFM as a main exposure adjusted for length, head circumference, sex, birth order, gestational age at birth, and child age at the 5-year follow up, maternal mental distress, presence or absence of grandmother living in the family, child living with or without biological parents, maternal age, parental education and family wealth index. This initial set of regression models with the same covariates structure were repeated by switching the main exposure from FM or FFM at birth to maternal BMI at birth or birth weight of the newborn to examine if previously reported relations were also replicated in our study. Furthermore, we also used FM or FFM measured at the 5-year follow up instead of FM or FFM at birth, as a main exposure to examine the relation when both the exposure and outcome variables measured at the same point in time.

Likewise, the second set of regression model contained standardized rate of FM or FFM accretion during early infancy as a main exposure adjusted for standardized rate of postnatal growth in length, length and head circumference at birth, child sex, birth order, gestational age, and child age at the 5-year follow up, maternal mental distress, presence or absence of grandmother living in the family, child living with or without biological parents, maternal age, parental education, and family wealth index.

Due to the exploratory nature of our study, we did not correct our models for multiple comparisons. Cut-off values are available for the SDQ to indicate probable emotional and behavioural disorders, but these cut-offs have not been validated in the Ethiopian context. Therefore, we just present mean SDQ scores.

Results

A total of 376 children were assessed for the outcome variable at the 5-year follow up, of whom 350 (93.1%) had complete data on all covariates (**Figure 1**). From those with complete data, 176 (50.3%) were females and 166 (47.4%) were first born. Birth weight (mean ± SD) was 3.0 ± 0.4 kg. FFM at birth was 2.8 ± 0.3 kg, and FM was 0.2 ± 0.2 kg. Age of the children at the 5-year follow up was 59.9 ± 1.5 months. About one-third (32.9%) of the mothers and 37.1% of the fathers had received secondary and above level of education. Maternal age at enrolment was 24.8 ± 4.7 years. Background characteristics between children followed and not followed up at 5 years of age were compared and no significant differences except birth order were found **(Table 1)**. The mean total difficulty score was 10.4 ± 5.8, while it was 5.7 ± 3.4 for internalising and 4.6 ± 3.7 for externalising scores **(Table 2).**

Relationship between BC and SDQ score

Birth weight showed no significant association with SDQ score. However, FFM at birth was a negative and FM a positive predictor of SDQ score among children at 5 years of age. Each additional kg of FFM at birth was associated with 3.94 points lower (β=-3.94; 95% CI -7.04, -0.83) SDQ score, after adjustment for neonatal and parental characteristics. Specifically, for each kg FFM at birth, there was 2.26 point lower (β=-2.26; 95% CI [-4.17, -0.34) in internalising problem score. On the other hand, for each kg FM tissue at birth, total SDQ score was 5.69 points (β=5.69; 95% CI 1.38,10.00) higher at 5 years of age. Specifically, for each kg FM at birth, there was a 3.30 points higher externalising behaviour problem score (β=3.30; 95% CI 0.64,5.95) at 5 years of age. **(Table 3)**.

There was no significant association between standardized rate of tissue accretion for FM or FFM during early infancy and SDQ score at 5 years of age. However, rate of FM accretion during early infancy (4-6 months) showed a positive association with externalising problem score at 5 years of age **(Table 4).**

Maternal BMI at birth was positively associated with SDQ score, whereas this was not the case for crude birth weight when each of them were included as main exposure instead of BC at birth or in early infancy. Furthermore, when BC at 5 years of age was included as main exposure instead of BC at birth, there was no association between FM or FFM and SDQ score at 5 years of age. (data not shown).

Role of covariates

Female sex was negatively associated with externalising problem score while length at birth was positively associated with SDQ score and internalising problem score. Living with non-biological parents was positively associated with externalising problem score. Higher maternal age (marginally associated), higher level of paternal education and higher level of parental wealth index were all associated negatively with higher score of SDQ at 5 years of age. **(Table 3).** Additional, adjustment to interviewers neither showed association nor changed the findings.

Discussion

In this study, we report the linear relationship between FM or FFM at birth and during early infancy, with mental health status of children at 5 years of age. FM at birth was positively and FFM was negatively associated with SDQ score while rates of postnatal FM or FFM accretion showed no association with SDQ score. Maternal BMI showed a positive association with SDQ score.

FFM tissue measured at birth showed a negative association with SDQ score and internalising problems at 5 years of age. In our previous report from the same cohort, FFM tissue at birth was associated positively with growth and cognitive development of children from 1-5 years of age (39,40). Based on the current and previous findings from this cohort (31,39–41), FFM tissue during fetal life consistently predicted better linear growth, cognitive and mental health outcomes of children. FFM accretion during fetal life may reflect the quality of intrauterine growth and maturation of the brain and nervous systems, both of which could have contributed to the cognitive, emotional and behavioural development of children early in life (14,15).

Foetal FM tissue accretion measured at birth showed a positive association with SDQ score and externalising problem score at 5 years of age. One previous study also reported a positive association between adiposity and higher SDQ score during early childhood (27), and higher risk of mental illness during adulthood (27). Other studies have reported birth weight and BMI of children to be positively associated with SDQ score of children (24,42). Among Australian children, obesity at 4 and 5 years of age was associated with a higher rate of poor peer-relationships and teacher-reported emotional problems of children at 8 to 9 years of age (42). Another longitudinal study reported BMI during early childhood was associated with later internalising problem starting from 1st grade of schooling but not among preschool children (43). Although there is a need for additional studies with a precise measure of BC, there is growing evidence that FM accretion and its proxy anthropometric indicators during early infancy and childhood predict risk of poorer mental health outcome in later life. Despite the lack of studies investigating potential underlying mechanisms, one hypothesis is that poor maternal nutritional status during pregnancy might interfere with fetal growth, resulting in elevated adiposity at birth (25,26) that may then contribute to poorer mental health outcomes at later ages (14,15).

Standardized rates of FM or FFM accretion during early infancy showed no association with SDQ score at 5 years of age. The observation that fetal rather than postnatal BC growth predicted the mental health status of children, may relate to the critical stages of brain development that occur during fetal life including the formation of neurons, neural tube structures, central and peripheral nervous system, and development of most of the cortical regions of the brain (44).

Our data however do not reveal any mechanisms that might explain the association of fetal but not infant tissue accretion with childhood mental health outcomes, but we suggest that prenatal FFM accretion may represent a proxy for optimal neurobehavioral growth and development, while prenatal FM accretion indicates constraint of investment in neurobehavioral development at this critical period. Further work on this issue may improve understanding of how environmental factors impact fetal programming of later health and disease (45).

Previous studies have reported higher maternal BMI during pregnancy (16,23) as well as low or high weight at birth (24,46) to be predictors of EBP of children during early life. Our results further clarified this issue. When maternal BMI at birth was included as a main exposure instead of BC in this study, higher maternal BMI showed a positive association with SDQ score. However, when the model was adjusted for FM or FFM at birth, the association disappeared.

Furthermore, when birthweight replaced the main exposures (FM and FFM), it showed no association with SDQ score. Our findings therefore support measuring BC precisely to identify specific predictors of childhood mental health. In addition, the relationship initially observed between maternal BMI during pregnancy and weight at birth with SDQ score may be mediated by FM or FFM at birth.

Female sex, child living with biological parent, higher family wealth index, higher maternal age and higher paternal education were found to be protective factors for SDQ score of children at 5 years of age. Since several of these are modifiable factors, they are important for designing potential interventions to improve childhood mental health.

One of the main strength of this study is the longitudinal assessment of BC using air displacement plethysmography (ADP) method in a relatively large sample. ADP is an accurate and precise measure of BC assessment method. The other strength of this study is that the exposure variables were measured at birth and during early infancy before the outcome was determined. One of the challenges in previous studies in examining the relation between proxy indicators of fat mass (adiposity, BMI or obesity) and mental health of children was the potential for reverse causality, in that some case-control or cross-sectional studies did not measure the outcome before the exposure. Internal reliability coefficient (Cronbach alpha) was 0.71 for SDQ score, which is within the acceptable range for reliability test.

Our study did have several limitations. We were not able to adjust to several determinants of mental health outcome including breastfeeding status and dietary intake, over the five-year follow up period. Loss to follow up was moderate. The psychosocial aspects of the father including substance use and depression were not measured. Assessment at a later childhood age might also be of interest. Parental report is also a widely used way of generating data from infant and young children with a higher degree of agreement with self or teacher report of the problem (47). Despite all these limitations, our finding provides new insight as to how growth and BC during fetal and infant life may relate to the mental health outcomes of young children. However, it is difficult to know the clinical significance of our findings because of unclear relationship between SDQ scores and clinical outcomes especially in low and middle-income countries.

In conclusions, fetal rather than infant FM and FFM were associated with mental health outcomes of children at 5 years of age. FM at birth predicted a higher and FFM a lower SDQ score. More studies on how early life BC affect mental health status of children are needed.

Acknowledgements

The authors would like to acknowledge Jimma University for arranging and facilitating the research setup. Most importantly, we like to acknowledge the research nurse for their unreserved commitment and the study participants for their time and participation.

Authors' contributions

HF, TG, PK, KFM, GSA, JW, MT and MA: designed the study; MA, BA, TG, MT, GSA, RW, PK and HF: conducted the study; MA and CR: analysed data and interpreted the finding; MT, TG, CH, RW, GSA, JW, PK and HF: commented on the interpreted findings and contributed to the write up; MA: wrote the first draft of the manuscript and had responsibility for the whole work. All authors reviewed the content, read and approved the final version.

None of the authors declared conflicts of interest

References

1. Darling-Churchill KE, Lippman L. Early childhood social and emotional development: Advancing the field of measurement. J Appl Dev Psychol. 2016 Jul;45:1–7.

2. Daelmans B, Darmstadt GL, Lombardi J, Black MM, Britto PR, Lye S, et al. Early childhood development: the foundation of sustainable development. The Lancet. 2017 Jan;389(10064):9–11.

3. Goodman A, Goodman R. Strengths and Difficulties Questionnaire as a Dimensional Measure of Child Mental Health. J Am Acad Child Adolesc Psychiatry. 2009 Apr;48(4):400–3.

4. Cortina MA, Sodha A, Fazel M, Ramchandani PG. Prevalence of Child Mental Health Problems in Sub-Saharan Africa: A Systematic Review. Arch Pediatr Adolesc Med. 2012 Mar 5;166(3):276–81.

5. Giel R, de Arango MV, Climent CE, Harding TW, Ibrahim HH, Ladrido-Ignacio L, et al. Childhood mental disorders in primary health care: results of observations in four developing countries. A report from the WHO collaborative Study on Strategies for Extending Mental Health Care. Pediatrics. 1981 Nov;68(5):677–83.

6. Anselmi L, Barros FC, Teodoro MLM, Piccinini CA, Menezes AMB, Araujo CL, et al. Continuity of behavioral and emotional problems from pre-school years to pre-adolescence in a developing country. J Child Psychol Psychiatry. 2008 May;49(5):499–507.

7. Hofstra MB, Van Der Ende J, Verhulst FC. Child and Adolescent Problems Predict DSM-IV Disorders in Adulthood: A 14-Year Follow-up of a Dutch Epidemiological Sample. J Am Acad Child Adolesc Psychiatry. 2002 Feb;41(2):182–9.

8. Breslau J, Miller E, Breslau N, Bohnert K, Lucia V, Schweitzer J. The Impact of Early Behavior Disturbances on Academic Achievement in High School. PEDIATRICS. 2009 Jun 1;123(6):1472–6.

9. McLeod JD, Uemura R, Rohrman S. Adolescent Mental Health, Behavior Problems, and Academic Achievement. J Health Soc Behav. 2012 Dec;53(4):482–97.

10. Currie J, Stabile M. Child mental health and human capital accumulation: the case of ADHD. J Health Econ. 2006 Nov;25(6):1094–118.

11. Hancock KJ, Mitrou F, Shipley M, Lawrence D, Zubrick SR. A three generation study of the mental health relationships between grandparents, parents and children. BMC Psychiatry [Internet]. 2013 Dec [cited 2017 Jul 6];13(1). Available from: http://bmcpsychiatry.biomedcentral.com/articles/10.1186/1471-244X-13-299

12. Olson SL, Ceballo R, Park C. Early problem behavior among children from low-income, mother-headed families: a multiple risk perspective. J Clin Child Adolesc Psychol Off J Soc Clin Child Adolesc Psychol Am Psychol Assoc Div 53. 2002 Dec;31(4):419–30.

13. Groen-Blokhuis MM, Middeldorp CM, van Beijsterveldt CEM, Boomsma DI. Evidence for a causal association of low birth weight and attention problems. J Am Acad Child Adolesc Psychiatry. 2011 Dec;50(12):1247–1254.e2.

14. Wiles NJ. Fetal Growth and Childhood Behavioral Problems: Results from the ALSPAC Cohort. Am J Epidemiol. 2006 Mar 1;163(9):829–37.

15. Chatterji P, Lahiri K, Kim D. Fetal growth and neurobehavioral outcomes in childhood. Econ Hum Biol. 2014 Dec;15:187–200.

16. Deardorff J, Smith LH, Petito L, Kim H, Abrams BF. Maternal Prepregnancy Weight and Children's Behavioral and Emotional Outcomes. Am J Prev Med [Internet]. 2017 Jul [cited 2017 Jul 25]; Available from: http://linkinghub.elsevier.com/retrieve/pii/S0749379717302702

17. Gene-environment interactions in mental disorders [Internet]. [cited 2017 Oct 19]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1414673/

18. Santos LM dos, Queirós FC, Barreto ML, Santos DN dos. Prevalence of behavior problems and associated factors in preschool children from the city of Salvador, state of Bahia, Brazil. Rev Bras Psiquiatr. 2016 Mar;38(1):46–52.

19. Treanor M. Social assets, low income and child social, emotional and behavioural wellbeing. Fam Relatsh Soc. 2016 Jul 7;5(2):209–28.

20. Norman RE, Byambaa M, De R, Butchart A, Scott J, Vos T. The Long-Term Health Consequences of Child Physical Abuse, Emotional Abuse, and Neglect: A Systematic Review and Meta-Analysis. Tomlinson M, editor. PLoS Med. 2012 Nov 27;9(11):e1001349.

21. Shonkoff JP, Deborah A. Phillips, editors. From neurons to neighborhoods: the science of early child development. Washington, D.C: National Academy Press; 2000. 588 p.

22. Morgane PJ, Austin-LaFrance R, Bronzino J, Tonkiss J, Díaz-Cintra S, Cintra L, et al. Prenatal malnutrition and development of the brain. Neurosci Biobehav Rev. 1993;17(1):91–128.

23. Bergmann S, Schlesier-Michel A, Wendt V, Grube M, Keitel-Kornd?rfer A, Gausche R, et al. Maternal Weight Predicts Children's Psychosocial Development via Parenting Stress and Emotional Availability. Front Psychol [Internet]. 2016 Aug 10 [cited 2017 Jul 5];7. Available from: http://journal.frontiersin.org/Article/10.3389/fpsyg.2016.01156/abstract

24. van Mil NH, Steegers-Theunissen RPM, Motazedi E, Jansen PW, Jaddoe VWV, Steegers EAP, et al. Low and High Birth Weight and the Risk of Child Attention Problems. J Pediatr. 2015 Apr;166(4):862–869.e3.

25. Ajuwon KM, Arentson-Lantz EJ, Donkin SS. Excessive gestational calorie intake in sows regulates early postnatal adipose tissue development in the offspring. BMC Nutr [Internet]. 2016 Dec [cited 2017 Sep 8];2(1). Available from: http://bmcnutr.biomedcentral.com/articles/10.1186/s40795-016-0069-3

26. Lau EY, Liu J, Archer E, McDonald SM, Liu J. Maternal Weight Gain in Pregnancy and Risk of Obesity among Offspring: A Systematic Review. J Obes. 2014;2014:1–16.

27. Davillas A, Benzeval M, Kumari M. Association of Adiposity and Mental Health Functioning across the Lifespan: Findings from Understanding Society (The UK Household Longitudinal Study). Meyre D, editor. PLOS ONE. 2016 Feb 5;11(2):e0148561.

28. Andersen GS, Girma T, Wells JCK, Kæstel P, Michaelsen KF, Friis H. Fat and Fat-Free Mass at Birth: Air Displacement Plethysmography Measurements on 350 Ethiopian Newborns. Pediatr Res. 2011 Nov;70(5):501–6.

29. Andersen GS, Girma T, Wells JC, Kaestel P, Leventi M, Hother A-L, et al. Body composition from birth to 6 mo of age in Ethiopian infants: reference data obtained by air-displacement plethysmography. Am J Clin Nutr. 2013 Oct 1;98(4):885–94.

30. Lakshmi S, Metcalf B, Joglekar C, Yajnik CS, Fall CH, Wilkin TJ. Differences in body composition and metabolic status between white UK and Asian Indian children (EarlyBird 24 and the Pune Maternal Nutrition Study). Pediatr Obes. 2012 Oct;7(5):347–54.

31. Abera M, Tesfaye M, Girma T, Hanlon C, Andersen GS, Wells JC, et al. Relation between body composition at birth and child development at 2 years of age: a prospective cohort study among Ethiopian children. Eur J Clin Nutr [Internet]. 2017 Sep 27 [cited 2017 Oct 5]; Available from: http://www.nature.com/doifinder/10.1038/ejcn.2017.129

32. Admassu B, Wells JCK, Girma T, Andersen GS, Owino V, Belachew T, et al. Body composition at birth and height at 2 years: a prospective cohort study among children in Jimma, Ethiopia. Pediatr Res. 2017 Aug;82(2):209–14.

33. Ballard JL, Khoury JC, Wedig K, et al: New Ballard Score, expanded to include extremely premature infants. J Pediatr 1991; 119:417–423. Reprinted by permission of Dr Ballard and Mosby—Year Book, Inc.

34. Servili C, Ferrari S, Hanlon C, Medhin G & Prince M. Maternal mental health as a predictor of adverse behavioural and emotional outcomes in pre-school age children: a population-based birth cohort study in rural Ethiopia. PhD Thesis.

35. youthinmind: What is the SDQ? http://www.sdqinfo.com/py/sdqinfo/b0.py: accessed: 10/5/2017.

36. Kessler RC, Green JG, Gruber MJ, Sampson NA, Bromet E, Cuitan M, et al. Screening for serious mental illness in the general population with the K6 screening scale: results from the WHO World Mental Health (WMH) survey initiative. Int J Methods Psychiatr Res. 2010 Jun;19(S1):4–22.

37. Tesfaye M, Hanlon C, Wondimagegn D, Alem A. Detecting postnatal common mental disorders in Addis Ababa, Ethiopia: Validation of the Edinburgh Postnatal Depression Scale and Kessler Scales. J Affect Disord. 2010 Apr;122(1–2):102–8.

38. Christiansen TB and Lauritsen JM. (Ed.) EpiData - Comprehensive Data Management and Basic Statistical Analysis System. Odense Denmark, EpiData Association, 2010-. Http://www.epidata.dk.

39. Abera M, Tesfaye M, Admassu B, Hanlon C, Ritz C, Wibaek R, et al. Body composition during early infancy and developmental progression from 1-5 years of age: The iABC cohort study among Ethiopian children. in press in BJN.

40. Admasu A, Ritz C, Wells J, Girma T, Andersen G, et al. Association of fat and fat-free mass accretion in infancy with linear growth in childhood: A prospective cohort study in Jimma, Ethiopia. In press- in the JN.

41. Body composition at birth and height at 2 years: a prospective cohort study among children in Jimma, Ethiopia : Pediatric Research : Springer Nature [Internet]. [cited 2017 Oct 15]. Available from: http://www.nature.com/pr/journal/v82/n2/abs/pr201759a.html

42. Sawyer MG, Harchak T, Wake M, Lynch J. Four-Year Prospective Study of BMI and Mental Health Problems in Young Children. PEDIATRICS. 2011 Oct 1;128(4):677–84.

43. Bradley RH, Houts R, Nader PR, O'Brien M, Belsky J, Crosnoe R. The relationship between body mass index and behavior in children. J Pediatr. 2008 Nov;153(5):629–34.

44. Stiles J, Jernigan TL. The Basics of Brain Development. Neuropsychol Rev. 2010 Dec;20(4):327–48.

45. Coe CL and Lubach GR. Fetal Programming Prenatal Origins of Health and Illness. Association for Psychological Science, 2008; 17(1).

46. Kelly YJ. Birthweight and behavioural problems in children: a modifiable effect? Int J Epidemiol. 2001 Feb 1;30(1):88–94.

47. Goodman R, Ford T, Corbin T, Meltzer H. Using the Strengths and Difficulties Questionnaire (SDQ) multi-informant algorithm to screen looked-after children for psychiatric disorders. Eur Child Adolesc Psychiatry. 2004 Jul 1;13(2):ii25-ii31.

Tables

Table 1: Child and parental characteristics at birth for those children followed and not followed up at 5 years of age

New born characteristics	**Followed up (n=350)**	**Not followed up (n=294)**	**P-value**
Sex			
Female sex	176 (50.3)	136 (51.1)	0.45
Birth weight (kg)	3.0 ± 0.4	3.0 ± 0.4	1.00
Fat free mass (kg)	2.8 ± 0.3	2.8 ± 0.4	1.00
Fat mass (kg)	0.2 ± 0.2	0.2 ± 0.2	1.00
Length (cm)	49.1 ± 2.0	49.0 ± 2.0	0.54
Head circumference (cm)	34.8 ± 2.3	34.7 ± 1.5	0.54
Birth order			0.01
First	166 (47.4)	171 (64.5)	
Second	96 (27.4)	51 (19.3)	
Third and above	88 (25.2)	43 (16.2)	
Parental characteristics			
Maternal education			0.89
Illiterate	25 (7.1)	18 (6.8)	
Primary school	210 (60.0)	164 (61.9)	
Secondary school and above	115 (32.9)	83 (31.3)	
Maternal age (years)	24.8 ± 4.7		
Paternal education			0.19
Illiterate	9 (2.6)	11 (4.4)	
Primary school	211 (60.3)	134 (53.8)	
Secondary and above	130 (37.1)	104 (41.8)	
Assessment at the follow up			
Age (month) at 5-year follow-up	59.9 ± 1.5		

Table 2: Distribution of the Strengths and Difficulties Questionnaire scores and the maternal common mental distress score; n=350

Variables	**Mean ± SD**
Total difficulty (EBP) score [a]	10.4±5.8
Emotional problem score [b]	3.2 ± 2.5
Conduct problem score [b]	1.9 ± 1.8
Peer problem score [b]	2.5 ± 1.5
Hyperactivity/inattention score [b]	3.1 ± 2.6
Prosocial score [b]	8.8 ±1.6
Internalizing problems score [c]	5.7±3.4
Externalizing behaviors score [c]	4.6±3.7
Common maternal distress score [d]	3.6±4.4

a: score computed out of 40 points, b: out of 10 points; c: out of 20 points; d: out of 24 points

Table 3: **Relation between fat (FM) or fat-free mass (FFM) at birth, and emotional and behavioural score at 5 years of age**			
Main exposures	Total difficulty score	Externalising subscale	Internalising subscale
FFM	-3.94 [-7.04,-0.83] *	-1.64 [-3.60,0.32]	-2.26 [-4.17,-0.34] *
FM	5.69 [1.38,10.00] **	3.30 [0.64,5.95] *	2.40 [-0.30,5.09]
Covariates			
Length at birth	0.62 [0.12,1.11] *	0.17 [-0.16,0.51]	0.42 [0.15,0.68] **
Female	-0.92 [-2.14,0.29]	-1.02 [-1.85,-0.19] *	0.08 [-0.63,0.79]
Maternal age	-0.19 [-0.39,0.02]	-0.10 [-0.24,0.03]	-0.085 [-0.19,0.02]
Lives with non-biological family	2.10 [-1.07,5.27]	2.41 [0.26,4.55] *	-0.29 [-1.97,1.38]
Paternal education			
No education	0	0	0
Primary level	-3.24 [-7.11,0.63]	-1.69 [-3.98,0.59]	-1.59 [-4.57,1.38]
Secondary and above	-4.49 [-8.62, -0.36] *	-2.18 [-4.62,0.26]	-2.41 [-5.50,0.68]
Wealth index			
1st quantile (poorest)	0	0	0
2nd quantile	0.30 [-1.71,2.30]	0.73 [-0.61,2.07]	-0.45 [-1.56,0.65]
3rd quantile	-0.88 [-2.83,1.07]	0.01 [-1.34,1.34]	-0.89 [-1.98,0.21]
4th quantile	-0.85 [-2.95,1.25]	0.43 [-0.93,1.79]	-1.28 [-2.57,0.02]
5th quantile	-2.19 [-4.32,-0.05] *	-0.24 [-1.63,1.15]	-2.04 [-3.27,-0.82] **
N	350	350	350
adj. R^2	0.06	0.02	0.07

Data are B-coefficients (95% confidence interval) from multiple linear regression analysis. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$
Models are adjusted for length, head circumference, sex, birth order, and gestational age all at birth and child age at the 5-year follow up, maternal mental distress, presence or absence of grandmother living in the family, child living with or without biological parents, maternal age, parental education and family wealth index .

Table 4: **Relation between rate of postnatal FM or FFM tissue accretion, and emotional and behavioural problem score at 5 years of age**

Main exposures	Total difficulty score	Externalising score	Internalising score
Rate of FFM accretion (0-6mo)	-0.32[-1.06,0.42]	0.06[-0.43,0.56]	-0.38[-0.81,0.05]
N	331	331	331
adj. R^2	0.04	0.01	0.07
Rate of FM accretion (0-4mo)	0.17[-0.48,0.82]	0.12[-0.34,0.57]	0.04[-0.32,0.41]
N	331	331	331
adj. R^2	0.04	0.01	0.07
Rate of FM accretion (4-6mo)	0.55[-0.10,1.20]	0.45 [0.03,0.86] *	0.11[-0.26,0.48]
N	313	313	313
adj. R^2	0.05	0.03	0.05

Data are B-coefficients (95% confidence interval) from multiple linear regression analysis. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$
Models are adjusted for, standardized rate of postnatal growth in length, length at birth, head circumference at birth, child sex, child age at the 5-year follow up, birth order and gestational age, maternal mental distress, presence or absence of grandmother living in the family, child living with or without biological parents, maternal age, parental education, family wealth index.