



Maternal nutritional status mediates the association between maternal age and birth outcomes

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Abstract

Young maternal age during pregnancy is linked with adverse birth outcomes. This study examined the role of maternal nutritional status in the association between maternal age and small for gestational age (SGA) delivery and birth length. We used data from a birth cohort study in Ethiopia, involving women who were 15–24 years of age and their newborns. A mediation analysis was fitted in a sample of 1,422 mother infant dyads for whom data on birth length were available, and 777 dyads for whom gestational age and birth weight was measured. We used commands, *medeff* for the mediation analysis and *medsens* for sensitivity analysis in STATA 14. Maternal nutritional status, measured by mid-upper arm circumference, mediated 21% of the association between maternal age and birth length and 14% of the association with SGA delivery. The average direct effect (ADE) of maternal age on birth length was ($\beta = 0.45$, 95% CI [0.17, 0.99]) and the average causal mediated effect (ACME) was ($\beta = 0.12$, 95% CI [0.02, 0.15]). We also found an ADE ($\beta = 0.31$, 95% CI [0.09, 0.47]) and an ACME of ($\beta = 0.05$, 95% CI [0.003, 0.205]) of maternal age on SGA delivery. The sensitivity analysis suggests an unmeasured confounder with a positive correlation of 0.15 and 0.20 between the mediator and the outcome could explain the observed ACME for birth length and SGA, respectively. We cannot make strong causal assertions as the findings suggest the mediator partly explained the total effect of maternal age on both outcomes.

KEYWORDS

adolescent pregnancy, birth cohort, infant growth, intrauterine growth retardation, maternal nutrition, nutritional epidemiology

1 | INTRODUCTION

Young maternal age during pregnancy is commonly linked with adverse maternal and child health outcomes (Borja & Adair, 2003; de

Abbreviations: ENGINE, Empowering New Generation to Improve Nutrition and Economic Opportunities; LMIC, low- and middle-income countries; MUAC, mid-upper arm circumference; SGA, small for gestational age.

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Vienne, Creveuil, & Dreyfus, 2009; Paranjothy, Broughton, Adappa, & Fone, 2009; Restrepo-Méndez et al., 2011; Sharma et al., 2008). An estimated 16 million adolescent women contribute to about 11% of all births worldwide. Of this, more than 95% occur in developing countries where early child marriage is a common practice (WHO, 2005). Adolescents and young people age 10–24 constitute up to 30% of the total population in Ethiopia. Although there are variations by area of residence, education and region, the median age of marriage for women is 16.1 years, and for majority of them, marriage drives their sexual debut then child birth. Once a girl is married, there are high expectations for her to bear a child soon after marriage (Federal Ministry of Health, 2015). A report from the 2011 Ethiopian Demographic and Health Survey (EDHS) indicated that 12% of adolescent girls aged 15–19 were already mothers or pregnant of their first child (Central Statistical Authority, 2012).

Early maternal age during pregnancy is linked to intrauterine growth retardation, low birthweight, preterm birth, child mortality, childhood stunting and maternal anaemia (Gibbs, Wendt, Peters, & Hogue, 2012). Several studies have attributed these associations to maternal sociodemographic, nutritional and psychosocial factors. (Gibbs et al., 2012; Markovitz, Cook, Flick, & Leet, 2005). Low economic status and suboptimal antenatal care are certainly more common in younger women compared with older ones. (DuPlessis, Bell, & Richards, 1997; Markovitz et al., 2005). Younger women are also less likely to go to school leaving them dependent on a minimum income to support their family. As adolescence is a period of significant growth (Chulani & Gordon, 2014; DuPlessis et al., 1997), continued growth during pregnancy could hence result in competition between the mother and fetus for important nutrients. Interference with foetal growth could increase the risk of adverse birth outcomes (Abu-Saad & Fraser, 2010; Leary, 2005). Where chronic maternal malnutrition is prevalent, the consequences of this competition are even more detrimental both to the mother and the fetus perpetuating malnutrition through generations (United Nations, 1993).

Studies indicated associations between young maternal age and adverse newborn birth outcomes after adjusting for various covariates (Borja & Adair, 2003; DuPlessis et al., 1997; Restrepo-Méndez et al., 2011). Other findings inform that these associations are due to poor maternal health and nutritional status (Borja & Adair, 2003; Fall et al., 2015; Gomez & Santolaya, 2005; Miller et al., 2016; Srinivasan, Satyanarayana, & Lukose, 2011). There however is considerable gap in knowing to what extent these associations are mediated through important exposures like maternal nutritional status during pregnancy. Most of the studies considered all of the exposures as confounders and did not examine the pathways through any of the covariates that maternal age would operate to result in adverse birth outcomes. Thus, we aimed to examine the role of maternal nutritional status in the association between maternal age and adverse newborn birth outcomes. We hypothesised that the association between maternal age and birth length and small for gestational age (SGA) delivery would be mediated through maternal nutritional status during pregnancy.

Key messages

- Young maternal age is associated with small for gestational age delivery and shorter newborn birth length
- Maternal nutritional status mediated 21% of the association between young maternal age and birth length
- Maternal nutritional status mediated 14% of the association between young maternal age and small for gestational age delivery
- An unmeasured confounder with a positive correlation of 0.15 and 0.20 between the mediator and the outcome could explain the observed mediated effect for birth length and SGA delivery, respectively

2 | METHODS

2.1 | Study setting, design and sample

Data used for this study were obtained from the Empowering New Generation in Nutrition and Economic opportunities (ENGINE) birth cohort study, which was conducted from January 2014 to March 2016 in the Oromia region of Ethiopia. Oromia region was selected purposively being the largest region in the country targeted by ENGINE. The three districts, namely, Goma, Woliso and Tiro Afeta were further selected from Oromia region based on (i) an expected population of more than 3,000 pregnant women so that we can account for loss to follow-up, (ii) geographical similarities in agroecology and agricultural production practices and (iii) proximity and accessibility. Trained data collectors who were nurses by profession, conducted a house-to-house active surveillance to recruit the study participants with support from health extension workers at the respective study sites. Upon identification, pregnant women who were at their second and third trimester were invited to enrol in the study after giving informed consent and were followed until delivery. Mothers with critical/chronic illness were not included in the study. A total of 1,422 pregnant women who were 15–24 years old and their newborns were included in the analysis to investigate mediational role of maternal nutritional status in the association between maternal age and birth length. For the second outcome, which was SGA delivery, infants whose birth weight was measured only within 72 h of delivery, and their gestational age was recorded were included in the analysis. Even though we had birthweight of the infants, gestational age at birth was not estimated for 645 of the participants which reduced the sample size to 777 in the analysis of the second outcome (SGA) (Figure 1).

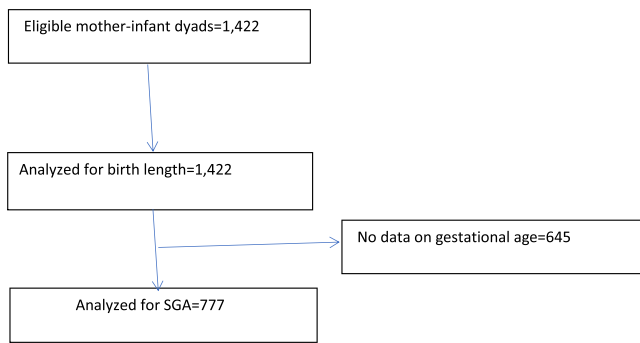


FIGURE 1 Flow diagram of study participants included in the analysis

2.2 | Measurements

Socio-economic and sociodemographic data were collected using a structured, interviewer administered questionnaire using Android tablet computer at recruitment. Anthropometric measurements were subsequently measured during the follow-up time and within 72 h after delivery. The main exposure in this study was maternal age during pregnancy. For majority of the newborns (93.6%) in the sample, anthropometric measurements were taken within 48 h, and the remaining proportion were measured in the third day. Length of the infant was measured in a recumbent position to the nearest 1 mm using a length board (Weigh and Measure LCC, USA), and unclothed birthweight was measured to the nearest 10 g using a digital weighing scale (SECA 876, Hannover, Germany). Mid-upper arm circumference (MUAC) of the women was measured during the second and early third trimester of their pregnancy on the left arm using midway between the olecranon and acromion processes using a non-elastic MUAC tape (SECA 201, Germany) (Cogill, 2003). In resource-poor settings, MUAC is a useful indicator to identify undernutrition during pregnancy since weight and height measurements are not accurate measurement due to changes in body shape and size. Its assessment is simple and can offer an advantage in identifying women at a higher risk of adverse birth outcomes. Despite a wide range of evidence indicating the association between lower MUAC and adverse health and birth outcomes among pregnant women, there has not been an established cut-off for identifying pregnant women who are undernourished. A recent review suggested a cut-off of 23 cm could have a higher specificity to identify pregnant women who are at risk of having a low birthweight (Tang et al., 2016), although it is at the expense of its sensitivity. A wealth index was constructed to control for wealth as a factor in maternal nutritional status and infant birth size, using the principal components analysis based on information on housing conditions, ownership of assets and availability of basic services (Filmer & Pritchett, 2001).

2.3 | Conceptual model and variables

Examining the pathways may better inform the mechanisms through which different exposures operate in resulting a certain outcome.

Intervening exposures, which link the causal pathway between main exposure and outcome, are commonly referred as mediators. In the current analysis, the variable considered to mediate the association between maternal age during pregnancy and birth length and SGA delivery is maternal nutritional status measured by maternal MUAC during pregnancy. The outcome variables were newborn length at birth measured in centimetres as a continuous outcome and SGA as a binary outcome. SGA was defined as gestational age specific birthweight lower than the 10th percentile in the WHO standard population (Kiserud et al., 2017). According to the potential outcome framework for a causal mediation analysis (Imai, Keele, & Tingley, 2010; VanderWeele, 2016), a simple mediation model can be presented as a mediator M (maternal nutritional status) in the pathway between exposure A (maternal age) and outcome Y (birth length and SGA), covariates C and unmeasured mediator-outcome confounder L (Figure 2). According to this approach, in order to properly identify average causal mediated effect (ACME) and average direct effect (ADE) of an exposure, the assumption of sequential ignorability (SI) must be met (Imai, Keele, & Yamamoto, 2010; VanderWeele, 2016). This assumption states that, first, the main exposure is assumed to be unrelated to potential unmeasured confounders. Next, the observed mediator is assumed to be unrelated to potential unmeasured confounders after the actual exposure and pre-exposure confounders are taken in to account. Since this assumption cannot be verified from the data by a statistical test, we conducted sensitivity analysis to examine the violation of this assumption (VanderWeele, 2016). Temporal relations between the mediator and the outcomes in this study have also been assured by measuring the mediator and the outcome at different time points of the study during the follow-up, the mediator preceding the outcome. The ACME will enable us to understand the relationship between the exposure and the outcomes via the mediator. The ADE expresses the direct effect of maternal age on birth length or SGA while maternal nutritional status not mediating. It may indicate all other mechanisms through which maternal age operates to cause the outcomes (Hicks & Tingley, 2011; VanderWeele, 2016).

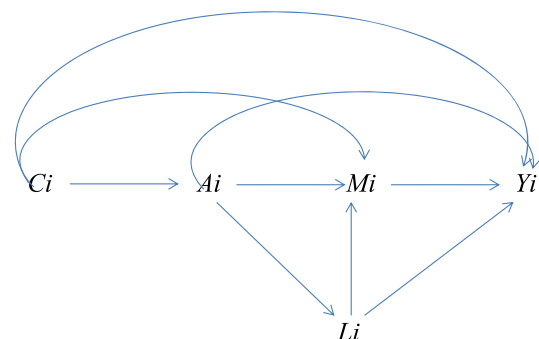


FIGURE 2 Conceptual model for the mediation analysis with exposure A (maternal age), mediator M (maternal nutritional status), outcome Y (birth length and SGA), covariate C and mediator-outcome confounder (unmeasured) L which itself can be affected by the exposure

2.4 | Statistical analysis

Exploratory analysis was performed to verify any missing values, outliers and normality before doing the main analysis. Descriptive data were reported as frequencies, percentages mean and standard deviations (SDs). The difference in maternal characteristics by the two outcomes; SGA and newborn birth length, were tested by χ^2 and Student's t-tests, respectively. Logistic and linear regression analyses were performed to assess the association between the main exposure (maternal age) and the outcomes (SGA and newborn birth length), respectively, adjusting for confounders. Then, in order to decompose the total effect of maternal age on the outcomes in to direct and mediated effects, we conducted a mediation analysis. In a preliminary analysis, to test the association between the exposure (maternal age), mediator (maternal nutritional status) and outcomes (birth length and SGA), a regression analysis was fitted, and the results indicated that there are statistically significant associations ($p < 0.05$) between them, supporting the mediational hypothesis. The method of potential outcome framework, as implemented in STATA 14 (StataCorp, Texas, USA), was used to estimate ACME and ADE. We used the Stata command *medeff* for the mediation analysis. Due to the strong assumption of SI, we used the *medsens* command to conduct sensitivity analysis to explore violation of the assumption due to the presence of unmeasured confounders and so that robustness of the results can be identified (Hicks & Tingley, 2011). The results of the sensitivity analysis were presented as the correlation between the error terms of the regression models for the mediator and outcome and the product of coefficient of determination of the two models. We specified linear regression for the continuous outcome (birth length) and a logistic regression for the binary outcome (SGA). Interaction between maternal age and maternal nutritional status was examined a priori and the interaction term was not significant with either SGA ($p = 0.60$) or birth length ($p = 0.41$) and was omitted from the regression models in the mediation analysis. The confidence intervals (CIs) were computed using a bootstrap estimation approach with 1,000 replications. All the

analyses were controlled for wealth score, maternal education, sex of the newborn, gestational age and parity for their potential confounding role. Both the main exposure and the mediator were entered in the model as continuous variables. The estimates are presented with their bias-corrected 95% CI. All tests were two side,d and statistical significance was declared at $p < 0.05$ in all the tests.

2.5 | Ethical issues

Ethical approval was granted from the Institutional Review Board of Jimma University and Tufts University before commencement of the study. Informed consent was obtained from the participants after a detailed explanation of the objectives of the study. During the study follow-up, mothers and newborns that had health problems were referred to a nearby health facility to seek proper medical care.

3 | RESULTS

The mean (\pm SD) age of the women was 20 years (± 2 years) with a mean MUAC of 23 cm (± 1.9). Mean birth length of the infants was 49.5 cm (± 2.24 cm) and 173 (22.3%) were delivered small for their gestational age. Differences in the outcomes by various maternal characteristics are illustrated in Table 1.

Mediation analysis of linear models for both the mediator and outcome (birth length) produced an ADE of maternal age ($\beta = 0.45$, 95% CI [0.17, 0.99]) and ACME of ($\beta = 0.12$, 95% CI [0.02, 0.15]). The estimate of ACME indicated that the effect of maternal age mediated through a change in maternal MUAC resulted in an increased birth length by 0.12. The total effect of increased maternal age, on average, increased birth length by 0.58 (total effect). The proportion of the total effect of maternal age mediated by maternal nutritional status was 21% (Table 2). A sensitivity analysis of the results informed that the assumption of SI can be violated ($ACME \neq 0$) in the presence of a positive correlation of 0.15 between the two error

TABLE 1 Birth length (cm) and SGA by maternal and child characteristics in a birth cohort study in rural Ethiopian

Variables	Birth length (cm), mean (SD) (N = 1,422)	p value	SGA [§] n = 777		p value
			Yes N(%)	No N(%)	
Educational status	No formal education	49.29(2.19)	61(24.3)	190(75.7)	0.635
	Primary	49.52(2.25)	96(21.2)	357 (78.8)	
	Secondary and above	49.76(2.28)	16(21.9)	57(78.1)	
Parity	Primi para	49.03(2.21)	88(27.3)	234(72.7)	0.004*
	Multi para	49.64(2.24)	85(18.7)	370(81.3)	
Wealth index	Lowest	48.99(2.30)	75(27.6)	197(72.4)	0.033*
	Middle	49.37(2.17)	43(19.6)	177(80.4)	
	Highest	50.10(2.09)	55(19.3)	230(80.7)	
Sex of child	Male	49.93(2.25)	80(21.3)	295(78.7)	0.547
	Female	49.11(2.21)	93(23.1)	309(76.9)	

Abbreviations: SGA, small for gestational age; SD, standard deviation.

[§]Statistically significant difference among groups at $p < 0.05$.

TABLE 2 Estimates of the mediation analysis with bias-corrected bootstrap confidence intervals for birth length and SGA delivery

Outcome	Mediator	Total effect	ADE	ACME	% mediated
Birth length (cm)	Maternal age	0.58(0.29, 0.94)*	0.45(0.17, 0.99)*	0.12(0.02, 0.15)*	21
SGA	Maternal age	0.31(0.09, 0.47)*	0.27(0.08, 0.44)*	0.05(0.003, 0.20)*	14

The model was adjusted for maternal education, wealth index, parity and infant sex.

Abbreviations: ACME, average causal mediated effect; ADE, average direct effect; MUAC, mid-upper arm circumference; SGA, small for gestational age.

*Statistical significance at $p = 0.05$

terms for the regression models fitting maternal MUAC and birth length as outcomes. Alternatively, the product of coefficient of determinations (R^2) method for the residual and total variance was also examined. The result indicated that an unmeasured confounder must explain 10% of the remaining variance in the mediator and 11% of the remaining variance in the outcome, $0.10 * 0.11 = 0.011$, for the ACME to be 0 (Table 3).

Mediation analysis of the relation between maternal age and SGA delivery through maternal MUAC produced an ADE ($\beta = 0.31$, 95% CI [0.09, 0.47]) and ACME of ($\beta = 0.05$, 95% CI [0.003, 0.205]). The result also indicated that maternal nutritional status mediated 14% of the total effect of maternal age on SGA delivery (Table 2). The result of the sensitivity analysis indicated that the assumption of SI could be violated in the presence of a positive correlation of 0.20 between the two error terms for the regression models fitting the mediator and outcome (Figure 3). The product of R^2 method also informed us that 21% of the remaining variance in the mediator and 19% in the outcome must be explained by the unmeasured confounders for a mediation through maternal nutritional status not to exist (ACME = 0) (Table 3).

4 | DISCUSSION

The preliminary analysis in the present study indicated that increased maternal age is associated with reduced odds of SGA delivery and increased newborn birth length as evidenced in previous researches (DuPlessis et al., 1997; Finlay, Ozaltin, & Canning, 2011; Ganchimeg et al., 2014; Gibbs et al., 2012). The mediation analysis has also identified that these associations were partly mediated through changes in maternal nutritional status during pregnancy. The mediator (maternal nutritional status during pregnancy) explained 21% and 14% of the total effect of maternal age on birth length and SGA delivery, respectively.

Nutritional status of young women could be deprived due to multitude of factors, endangering healthy development of the fetus.

TABLE 3 Results of the sensitivity analysis with the products of R^2 method for both SGA and birth length

Sensitivity results	Outcomes	
	Birth length (cm)	SGA delivery
Rho at which ACME = 0	0.1492	0.200
$R^2_M * R^2_Y$ at which ACME = 0:	0.0119	0.040
$R^2_M \sim R^2_Y$ at which ACME = 0:	0.0106	0.031

Younger women, due to suboptimal nutritional practices and poor environmental exposures are prone to undernourishment during their pregnancy (Haas et al., 2005; Markovitz et al., 2005). Moreover, pregnancy during adolescence, when nutritional demands are higher due to both the pregnancy and continued physical growth of the women, negatively affects birth outcomes. These consequences get even worse in settings where chronic malnutrition is rampant and maternal nutritional needs cannot be met, affecting foetal growth and development and also postnatal infant growth (Abu-Saad & Fraser, 2010; Chulani & Gordon, 2014; Leary, 2005).

Maternal undernutrition in late gestation is strongly associated with placental and foetal weights, depriving optimal development of the fetus (Bhutta et al., 2017). It is also evident that undernourished adolescent mothers face greater risks during pregnancy and childbirth, and their children set off on a weaker developmental path, both physically and mentally. It is directly linked to intrauterine growth retardation (IUGR), which results in low birth weight, prematurity and low nutrient stores in infants (Fekadu Beyene, 2013). In addition, undernutrition during pregnancy has intergenerational effect resulting deleterious health impacts in the population of countries where undernutrition is prevalent (Black et al., 2013; Black et al., 2013). It is one of the leading causes of maternal mortality and adverse birth outcome and is still a big challenge in most developing countries (Maduforo, Nwosu, Ndiokwelu, & Obiakor-Okeke, 2013).

Early and narrowly spaced pregnancies are among the causes triggering undernutrition in pregnant women in low- and middle-income countries (LMICs) increasing the risk of poor birth outcomes (King, 2003). Adolescent childbearing is a cross-cutting public policy topic which is closely associated also with multitude of social issues, including poverty, low economic status, health and mental health. The national adolescent and youth health strategy of Ethiopia mainly focuses on addressing some of the social, economic, educational and health problems faced by adolescent girls (Federal Ministry of Health, 2015). In light of the findings from the present study, there is a need for a far-reaching strategy to address nutritional needs of adolescent pregnancies along with other sexual and reproductive health interventions aimed at preventing early marriage and pregnancy.

5 | STRENGTH AND LIMITATIONS

We applied an analysis approach which has strong assumptions in order to evaluate robustness of the results using relatively large

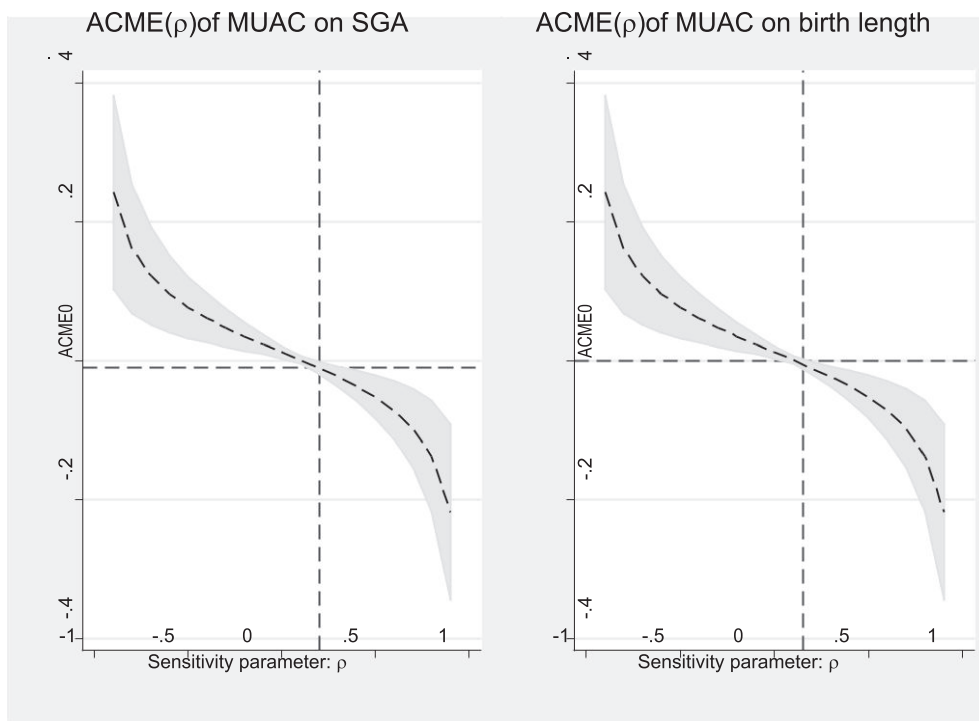


FIGURE 3 Graphical presentation of the results from the sensitivity analysis

sample. To the best of our knowledge, this is the first research work implementing a mediation analysis to understand the role of nutritional status in the relation between young maternal age during pregnancy and newborn birth outcomes in Ethiopia. As a limitation for this study, assessment of gestational age was based on maternal reporting of last normal menstrual period which might affect the estimation of SGA deliveries. A more reliable method of assessment using early trimester ultrasound is recommended for future studies. Similarly, the use of MUAC as a marker for nutritional status among adolescent mothers can be affected by their continued growth.

6 | CONCLUSION

This study found that maternal nutritional status partly mediated this association between maternal age and newborn birth length and SGA delivery. Although we are not able to make strong causal assertions, it is evident from the findings that the examined mediator partly explained the total effect of maternal age on both outcomes measured. However, the results need to be interpreted with caution as the sensitivity analysis suggested that any unmeasured confounder with a fairly weak correlation between the outcomes and the mediator can explain the observed results. The result also suggests that promotion of optimal nutritional status is important among young pregnancies in order to decrease adverse newborn birth outcomes. Beyond this, prevention of early marriage and pregnancy is important in order to avert the intergenerational consequences of adverse nutritional and health outcomes.

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CONFLICTS OF INTEREST

Authors declare that they have no conflicts of interest.

CONTRIBUTIONS

AW: Conceived and designed the protocol, analysed the data, interpreted the results and wrote the manuscript. TB, PK, SG, AR, AA, CL: Assisted in data analyses, the interpretation of the results and reviewing the manuscript. All authors have seen and approved the final version of the manuscript.

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