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Relations between mode of birth delivery and timing of developmental milestones and adiposity in preadolescence: a retrospective study

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Abstract

Background: Cesarean delivery (CS) is an increasingly common mode of delivery comprising over 30% of all deliveries in the U.S. The long-term impact of this delivery mode on child development remains unclear.

Aims: We investigated the relationship between mode of delivery (vaginal vs. CS) and timing of developmental milestones and adiposity in preadolescence, as well as additional milestones beyond motor/language development including toilet training, dressing, and feeding self.

Study Design: This study utilized a retrospective survey given to a parent/guardian and dual energy x-ray absorptiometry in preadolescence, respectively. A composite z-score was calculated based on nine questions pertaining to developmental milestones i.e., parent-reported age for supporting head by self, rolling over, sitting up, standing, walking, talking, toilet-training, dressing, and feeding self.

Subjects: 7–10-year-old ($N=104$) children in XXXX, XX

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Outcome Measures: Composite z-score for timing of attainment of developmental milestones, mode of delivery, and preadolescent adiposity.

Results: Vaginally-born children had a lower composite z-score, signifying earlier attainment of developmental milestones, relative to both emergency and planned CS-born children. Further, elective CS-born children had greater adiposity in preadolescence, relative to vaginal and emergency cesarean-section born children.

Conclusions: These findings suggest relationships between delivery mode, developmental milestones, and obesity in preadolescence. Additionally, they provide novel insights into the differential impact of elective versus emergency CS.

Keywords

Mode of Delivery; Birth Method; Cesarean Section; Vaginal Delivery; Developmental Milestones; Language Development; Gross Motor Development

INTRODUCTION

Cesarean section (CS) delivery births have become an increasingly common mode of delivery, comprising over 30% of all deliveries in the United States and up to 80% in other countries (1). Although historically CS births were reserved for emergency situations, numerous families and doctors routinely schedule CS for a variety of non-medical purposes. Relative to a vaginal birth process, undergoing elective CS results in a drastically different environmental, hormonal, and physical exposure for the newborn infant. For example, mother-infant transmission of microbiota occurs during vaginal delivery and significant differences in microbiota composition in infants delivered by CS compared to vaginally born infants have been previously demonstrated (2). The microbiota of newborn infants after emergency CS, however, more closely matches that of the mother, potentially due to membrane rupture and exposure to vaginal microbiota prior to CS (3). However, the extent to which delivery mode affects long-term markers of childhood development and health remains inadequately characterized.

However, the role of birth delivery mode on developmental milestones remains unclear. Motor development is a major part of the developmental pathway of a child. It is the process through which children acquire movement patterns and skills and involves: neuromuscular maturation; physical growth and behavioral characteristics of the child; the tempo of physical growth, biological maturation, and behavioral development; the residual effects of prior movement experiences; and the new movement experiences (4). Studies have shown that earlier acquisition of motor capabilities can enhance cognitive and language development and can predict working memory and processing speed in later childhood (5,6). Other studies have shown that developmental delay is associated with problems with later education and subsequent diagnosis of a learning disability (6). Previous population level longitudinal studies indicate that for every month earlier a child learned to stand, there was an average gain of one half of an intelligence quotient point (6). Similarly, later speech development was related to lower likelihood of progressing beyond basic education (6). Further, early motor development assessed prospectively at 1 year of age is associated with

superior executive function, increased gray matter density in the premotor cortex, striatum, and cerebellum, and increased white matter density in the frontal and parietal lobes at ages 33–35 years (7). Therefore, evidence from longitudinal studies suggests that motor development in early life may have a lasting impact on children's long-term physical development. However, the influence of birth delivery mode on developmental milestones remains unclear.

In addition to developmental milestones in infancy and toddlerhood, the implications of birth delivery mode on health markers in later childhood are inadequately characterized. Specifically, the extent to which birth delivery mode may influence risk for childhood obesity is unclear. Previous epidemiological studies present a conflicting body of literature with several studies indicating that CS is related to higher risk for obesity (8) while others have not observed a significant influence of CS (9). Additionally, most previous studies rely on BMI as the marker of obesity rather than whole body adiposity or other measures of fat distribution (e.g., subcutaneous abdominal adiposity and visceral adiposity). Quantifying the degree of whole body adiposity and patterns in fat distribution has greater clinical significance over BMI, which is a proxy measure of adiposity and does not distinguish between fat and fat-free mass.

Indeed, researchers examined whole body percent fat, fat mass, and lean mass using bioimpedance in 436 children and observed that children born via CS had a 46% higher risk of obesity at the age of 7 years (10). Therefore, mode of delivery may have lasting impact on developmental milestones and growth trajectory of children. Further, to gain a comprehensive understanding of adiposity-related health risk, it is important to assess fat distribution or abdominal adiposity tissue as well. Excess abdominal adiposity, and visceral fat mass in particular, has been mechanistically linked to a variety of markers of metabolic dysfunction including insulin resistance, obesity-related inflammation, and stress hormones (11). In addition to metabolic dysregulation, direct and proxy measures of abdominal adiposity in adults have been associated with greater risk of poor brain health including increased risk for neuroinflammation and dementia in later life (12). Thus, given the limited evidence linking CS birth to higher BMI, it is important to determine whether vaginal or CS birth is differentially related to whole body and abdominal adiposity in childhood.

Examining the importance of delivery mode for long-term development is grounded within a broader theoretical framework which posits that biological events or experiences in early life have long-term consequences for children's health (13). However, to our knowledge, previous work has not directly examined the relation of birth delivery mode to timing of developmental milestones and adiposity among preadolescent children. Further, considering the differences in early life microbial exposures, it is possible that CS birth implications for developmental milestones and childhood obesity are influenced by type of cesarean (i.e., elective vs. emergency). Accordingly, the present study examined the influence of birth delivery mode (i.e., vaginal vs. CS) on measures of language and motor development and adiposity in preadolescence. We hypothesized that compared to vaginally-born children, CS-born children would exhibit later achievement of developmental milestones and have greater adiposity in preadolescence. Among infants born by CS, we hypothesized that elective CS

would exhibit later achievement of developmental milestones and have greater adiposity in preadolescence compared to those born by emergency CS.

METHODS

Participants

The sample was comprised of preadolescent children (age 7 to 10 years) who previously participated in two large randomized-controlled trials between 2008–2017 ([Clinicaltrials.gov](https://clinicaltrials.gov) identifiers NCTXXXXXXX and NCTXXXXXXX) examining the influence of a 9-month physical activity afterschool program (XXXXXX study) on cognitive function and brain health among preadolescent children. The sample was further supplemented with additional children who only participated in the procedures identical to the FITKids baseline testing (2015–2017). Participants provided written assent and their legal guardians provided written consent in accordance with the ethical standards and regulations of the Institutional Review Board (IRB) at the XXXXXXX.

Procedure

Testing took place over two separate laboratory visits. During the first visit, participants completed informed assent/consent and height and weight were measured to calculate BMI. Concurrently, parents completed a Demographic and Health History Questionnaire, which was used to assess socioeconomic status (SES). SES was determined from eligibility for school meal-assistance programs, maternal and paternal education levels, and the number of parents with full-time employment. During the second visit, participants completed a dual-energy x-ray absorptiometry (DXA) assessment to assess whole body fat mass percentage (%Fat). Parents were contacted between 2015–2016 to complete a retrospective survey regarding pregnancy outcomes, early life nutritional intake, and the developmental milestones. The survey was disseminated and administered via an online platform (Qualtrics, Provo, Utah).

BMI and Adiposity Assessment

Participants' height was measured using a stadiometer (model 240; Seca, Hamburg, Germany) and weight was measured using a Tanita WB-300 Plus digital scale (Tanita, Tokyo, Japan). Each measurement was repeated three times and the average values were used for analyses. BMI was calculated as weight in kilograms adjusted for height in meters squared (kg/m^2). Whole body fat mass (%Fat) was measured using DXA with a Hologic Discovery A bone densitometer (software version 12.7.3; Hologic, Bedford, MA). Abdominal adiposity measurements are estimated in the program by placing a 5-centimeter-wide section across the entire abdominal region at a level approximately even with the fourth lumbar vertebrae and extending down to the top of the iliac crest. This section is defined as the region of interest (ROI). Total abdominal adipose tissue (TAAT) was defined as the total adipose tissue in the ROI. Subcutaneous abdominal adipose tissue (SAAT) was then determined by an algorithm that assesses the adipose tissue on the sides of the abdomen and estimates the amount of subcutaneous fat overlying the abdominal cavity. Visceral adipose tissue (VAT) was estimated by subtracting SAAT from TAAT.

Developmental Survey

A pediatric health history survey was developed by incorporating items from a previously validated questionnaire used in the All Our Babies study (14). Additional questions were adopted from medical intake forms from the National Institute of Mental Health and the Massachusetts Institute of Technology Medical Department. The online survey was disseminated to parents of previous FITKids participants between 2015 and 2016. Respondents included 4 fathers and 100 mothers. Survey questions pertained to mode of delivery (i.e. vaginal or CS [emergency vs. planned]) and the age at which children reached developmental milestones including: when they could support their head, roll over, sit up, stand alone, walk, talk, dress themselves, feed themselves, and when they were toilet trained. A composite z score was calculated based on the sum of the 9 individual items to index overall developmental milestone timing.

Other questions included gestational age, birth weight, maternal height and weight both preconception (used to calculate maternal BMI) and end of pregnancy (used to calculate total weight gain), number of previous births, and early life nutrition (i.e. breastfeeding or formula feeding) and duration. Reported birth weight, gestational age, and sex were all necessary in order to calculate percentiles for weight-for-gestational-age, which was calculated using the Fenton Growth Chart (15).

Previous research has demonstrated that retrospective survey techniques are a validated and reliable source of data for early life health history. In a study of twins assessing the reliability of a mailed survey recall, parents were able to accurately recall the age at which their children sat without support, crawled, rolled over, and walked without support (16). In another study, mothers were able to reliably recall infant motor milestones at their well-baby visit two-years after birth (17). Another study with 387 children found that mother's accurately recalled their child's attainment of eight significant developmental milestones three-years after birth (18). When comparing reported "age walked alone" with hospital records of 252 children, agreement coefficient was 0.84 two years after birth (19). There is additional evidence supporting maternal recall reliability for gestational age up to three years after birth (20), birth weight up to 30 years after birth (20), and early feeding events up to 15 years after birth (21).

Statistics

Consistent with national rates, the number of children in this study born vaginally (n=162) exceeded the number of children from CS (n=65). Therefore, children were matched by yoking for mode of delivery and gestational age. Independent sample t-tests were used to evaluate group differences (vaginal birth vs. CS) in the composite z score for timing of developmental milestones. Similar analyses were conducted for each of the nine different developmental milestones. CS was further bifurcated into elective and emergency CS groups. All vaginal deliveries were selected based on unassisted (i.e. no forceps or vacuum) vaginal births. One-way ANOVA and Bonferroni corrected *post hoc* tests were used to evaluate the group differences in timing of developmental milestone achievement, BMI, and adiposity variables across mode of delivery groups (vaginal vs. elective CS vs. emergency CS).

RESULTS

A total of 227 parents responded to the survey, with 162 unassisted vaginal births and 65 CS births. When yoking for birth mode and gestational age, two groups were formed with 52 children in each group. Gestational age was matched in both groups and children were included regardless of term status (range 32 to 42 weeks). Participant characteristics based on delivery mode are described in Table 1. Aggregating all groups, the average developmental timing for all nine milestones was within the anticipated range, based on the CDC milestone references (22). However, examining the groups separately based on delivery mode, the average milestone timing of the children born vaginally was approximately 1 month earlier than expected ranges in several milestones including timing for sitting up, walking, talking, and feeding self. Groups were not statistically different in other potential confounders of development such as sex, birth weight, weight-for-gestational age percentile, maternal BMI pre-conception, feeding type (i.e. breastfeeding vs. formula feeding), and duration of breast/formula feeding. The groups were not statistically different in age and SES in preadolescence. This descriptive information is included in Table 2.

Results of the ANOVA with Bonferroni corrections are presented in Figures 1 and 2. Vaginally-born children had a significantly lower developmental z score relative to both CS emergency (−0.65; 95%CI, −1.20 to −0.13) and CS elective (−0.89; 95%CI, −1.45 to −0.32) children. However, there were no significant differences in developmental timing z score between the emergency and elective CS-born (−0.24; 95%CI, −0.87 to 0.39) children. Relative to the vaginally-born children, children who were born by emergency CS were slower to stand alone (1.11mo; 95%CI, −2.22 to −0.01), walk (1.28mo; 95%CI, −2.55 to −0.02), and talk (4.05mo; 95%CI, −7.23 to −0.88). Similarly, children born by elective CS took longer to talk (3.60mo; 95%CI, 0.17 to 7.04), feed (5.26mo; 95%CI, 2.04 to 8.49), and dress (7.01mo; 95%CI, 2.28 to 11.75) themselves. Comparisons between the two CS groups revealed no significant differences in the timing of developmental milestones.

%Fat and adiposity differences are presented in Figures 3 and 4. There were no significant differences between the vaginally and emergency CS-born children in BMI or any of the adiposity measures in preadolescence. However, relative to vaginally-born children, those born via elective CS had significantly higher %Fat (4.72%; 95%CI, 0.08 to 9.35). Further, comparisons between emergency vs. elective CS-born children revealed that elective CS-born children had significantly higher BMI (3.23kg/m²; 95%CI, 0.50 to 5.96), %Fat (5.21%; 95%CI, 0.08 to 10.34), SAAT (466.67g; 95%CI, 124.78 to 808.57), and TAAT (523.96g; 95%CI, 132.56 to 915.34). However, no significant differences were observed between groups in regard to their VAT in preadolescence (57.27g; 95%CI, −11.45 to 126.01).

DISCUSSION

The work presented herein utilized a retrospective approach to determine the relationship of birth delivery mode on children's timing of motor developmental milestones and adiposity in preadolescence. Consistent with our *a priori* hypothesis, vaginally-born children reached developmental timing earlier across several milestones, relative to their CS-born counterparts. Interestingly, differential patterns were observed whereby children who were

born by emergency CS stood, walked, and talked later than vaginally born children, but they caught up and were the same for self-feeding and self-dressing; whereas the elective CS group was the same for standing and walking, but fell behind for talking, self-feeding, and self-dressing. Regarding adiposity in childhood, there were no significant differences between vaginally and emergency CS-born children across any of the measures. However, elective CS-born children had significantly greater whole body and abdominal adiposity, relative to both the vaginally and emergency-born CS children. These findings point to the potentially lasting relationship between delivery mode and timing of developmental milestones in early childhood as well as the risk for excess adiposity in preadolescence.

Elective CS is scheduled ahead of time and takes place before labor begins. This is usually requested by mother or physician, or perhaps because of an underlying medical condition of either mother or fetus (23). Elective CS may provide benefits to both baby and mother. Considering the risk of several types of adverse neonatal outcomes increases after 39 weeks of gestation, elective CS performed at 39 weeks could decrease stillbirth and neonatal death (24), decrease the risk of aspiration of meconium and need for neonatal intubation (25), and reduce the rate of birth injuries such as fractures and nerve injuries by more than 50% (26).

In the mother, elective cesarean may reduce the risk of urinary incontinence and pelvic-organ prolapse from 10% to 5% (27). Additionally, elective CS helps to avoid the possibility of emergency CS, which is associated with substantial increases in morbidity and mortality (28). The relative risk of mortality of CS compared to vaginal delivery is 5:1 and the relative risk of elective CS compared to emergency CS is 1.5:1 (28). Emergency CS is performed if there is a complication during labor such as preeclampsia or fetal distress. Thus, infants born by emergency CS are usually exposed to vaginal microbiome after membrane rupture, and infants born by elective CS are not (2). Choice of delivery mode also results in different physiological experiences for the mother. For example, during emergency CS, mothers begin to experience pains and hormonal responses consistent with typical labor, whereas mothers undergoing elective CS face a considerably different endocrine milieu since the body does not undergo an increase in labor-related oxytocin release (6). This could explain the differences between the elective and emergency CS groups in our sample.

Additionally, there are a variety of known complications associated with CS. In a study examining UK data on 153,939 elective procedures, it was found that elective CS has a 2.84 fold greater chance of maternal death than from a vaginal birth (29). There are also increased risks of iatrogenic infection, scarring of the uterus, decreased fertility, miscarriage, ectopic pregnancy, placenta abruption, and placenta previa (30). Along with maternal risk, there is lifelong risk to the child. As the rates of CS have increased, so too have the rates of type I diabetes mellitus (23% higher (31)), Crohn's disease, multiple sclerosis, asthma (20% higher (31)), allergic rhinitis, and atopic dermatitis (31). Additional immune-related diseases that have been found to be associated with CS delivery include systemic connective tissue disorders, juvenile arthritis, inflammatory bowel disease, celiac immune deficiencies, and leukemia (32). Interestingly, another study found that children born by CS were at higher risk for asthma development, but children born by CS before membrane rupture (i.e. before labor began) were at higher risk for developing asthma than children born by CS after membrane rupture (i.e. after labor began) (33).

While it has been established that CS carries risk to both mother and child health, there is little information on whether that risk extends to the developmental trajectory in early childhood and obesity risk in later childhood. Motor development is a major part of the developmental pathway of a child. Piaget's Developmental Theory suggests that the development of sensorimotor systems is the first stage of cognitive development where children learn the logic of action and spatial reasoning. By his reasoning, action through motor development is the precursor to mental representation.

One study by Al Khalaf et al. (2015), found that children born by elective CS faced a delay in cognitive and motor development at 9 months of age and up to the first three years of age (34). They examined 11,134 infants at 9 months and again at 3 years. Parents completed the Ages and Stages questionnaire (ASQ) at 9 months and the Strengths and Difficulties questionnaire at 3 years (SDQ). The ASQ is designed to assess child development of communication, problem solving, personal social, gross motor, and fine motor skills. The SDQ is designed to assess emotion and behavioral problems. Children born by elective CS had 20% increased odds of having an abnormal communication score, 24% increased odds of delay in personal social development, and 62% increased odds of abnormal gross motor function. Children born by emergency CS had 8% increased odds of abnormal communication and 30% increased odds of abnormal gross motor function. There were no significant differences in the SDQ at age 3. However, although CS birth has been related to delays in general motor development, little is known regarding the timing of specific milestones. Since Al Khalaf and colleagues did not examine timing of the developmental milestones examined in our study, we are unable to directly compare/contrast with the findings of the current study. Nevertheless, in ranking attainment, Al Khalaf and colleagues similarly found that children who were born via Elective CS had the highest odds of delay or abnormal score, followed by Emergency CS, and Vaginal birth.

To our knowledge, the present findings are the first to reveal relations between delivery mode and timing of attainment of developmental milestones. Further, the present work examined both emergency and elective CS and observed that, relative to vaginally-born children, CS-born children exhibited slower attainment of developmental milestones, irrespective of type of CS. Specifically, children who were born by emergency CS were slower to attain the earlier milestones of standing alone, walking, and talking, but they caught up to their vaginally born counterparts in the later milestones of feeding self and dressing self. In contrast, the elective CS children stood alone and walked at the same time as the vaginally born children, but they began to fall behind and developed later in talking, feeding self, and dressing self. Especially with the differences emerging in later development for elective CS children, additional work is necessary to elucidate the impact of later attainment of the specific milestones studied here and subsequent language, motor, and cognitive development and function.

The mechanisms underlying motor development and later cognition are not well understood. One possibility that has been examined is that a subset of the neural systems that support the development of gross and fine motor skills during infancy also contribute to some cognitive processes in later life (6). Interestingly, Murray et al. found that infant development is associated with later general intellectual function and that the effect is not only found in the

late developers but is found even within the reference range of development indicating that a faster attainment of developmental milestones is related to better performance in executive function tasks as an adult (6). Other studies indicate that the early development of functional connections between the frontal cortex and basal ganglia lead to the early development of motor skills as well as improved frontal and subcortical structure, which could improve brain function later in life (35). This is supported by evidence that adult brain volume in the frontal cortex, basal ganglia, and cerebellum is directly related to the speed of infant motor development (7).

Although the work presented here is consistent with previous research, it is not clear how CS mode of delivery directly impacts subsequent timing of developmental milestones. Maternal BMI pre-pregnancy also plays a role in childhood development. In a study with 4,901 infants and mothers, compared to infants born to healthy-weight mothers, infants born to mothers with obesity were slower to sit unsupported and to crawl (36). The present study matched groups for maternal BMI in order to control for this factor. Other factors that could play a role in reaching developmental milestones include sex, where girls learn to stand faster than boys, but boys walk earlier than girls; and children of a lower SES may be delayed in standing without support than those of a higher social class (37). Learning to stand unsupported and to walk can be explained by gestational age, birth weight, maternal age, and sex of the child (37). Planned birth before 40 weeks of gestation is independently associated with poor child development, with each week before 40 weeks increasing risk, and is exacerbated by mode of birth other than vaginal birth even among low-risk pregnancies (38).

In addition to developmental delay, it has also been proposed that delivery mode may contribute to long-term risk for obesity. For example, previous research has documented an increased risk of obesity in adulthood for children born by CS (39). Goldani et al. (2011), had records of 2,057 subjects with type of delivery, birth weight, maternal smoking, and schooling after birth. A follow up with those subjects 23–25 years later indicated that the obesity rate in adults born by CS was 15.2%, whereas those born by vaginal delivery were at 10.4%, and this remained significant after other risk adjustments (39).

Although a comparatively smaller sample size, our findings are consistent with this previous work indicating greater obesity risk among CS-born children. Interestingly, the proportion of children in the overweight/obese category (i.e., 85%tile BMI-for-age) was almost two-fold greater among the elective CS group in our sample, relative to the vaginal and emergency CS-born children. Therefore, these data provide novel insights into the influence of CS-birth on obesity in childhood since the detrimental influence of CS may be selective for children who undergo the elective version of the procedure.

Another novel aspect of the present work is the assessment of whole body adiposity as well as fat distribution. Excess adiposity, particularly abdominal adiposity, is associated with greater systemic inflammation and metabolic dysregulation (11). Although VAT has received considerably more attention as a more metabolically pathogenic fat depot, SAAT has also been associated with higher circulating inflammatory and oxidative stress biomarkers even after adjustment for age, sex, smoking, physical activity, menopause, hormone replacement

therapy, and alcohol use (40). The results of the present study revealed that only children born via elective CS, and not emergency CS, exhibited increased %Fat and SAAT. The underlying mechanisms by which elective CS-birth may contribute to excess accumulation of fat mass in later childhood is unknown. However, candidate mechanisms may include the potentially lasting programming impact imparted by the vaginal microbiome on either predisposition to accumulate fat mass or increased likelihood of engaging in dietary behaviors that promote excess food consumption (9).

Studies also show that the microbiome of the infant is impacted by the mode of delivery (2). There is minimal microbial exposure to the infant in utero; instead, the birthing process provides exposure to vaginal and fecal microbes, in the case of vaginal delivery and to lesser extent emergency CS, or skin microbiome, in the case of elective CS-born infants. The hygiene hypothesis states that improper bacterial exposure in early life contributes to a greater risk of immune disease development. This would mean that vaginal delivery would impart a different microbiome (i.e. vaginal microbiota) than CS (i.e. skin bacteria) (31). Another potential mechanism may involve epigenetic modifications determined by experience-driven modification in gene expression. Epigenetics encompasses the study of changes in gene expression that may occur due to behavioral or environmental factors that are heritable but do not entail a change in DNA sequence (41,42). Pertinent to the work herein, infants born via elective CS have been previously shown to have higher DNA-methylation, a marker of epigenetic regulation, in white blood cells compared with that of those born vaginally (43). Interestingly, DNA methylation in key genes has also been implicated in childhood obesity risk. (44). Therefore, differences in genomic DNA-methylation around birth could serve as molecular mechanisms for later differences in disease risk associated with mode of delivery (43). Finally, future longitudinal studies examining changes in microbiome, epigenetic regulation, and body composition beginning at birth are necessary to determine the direct mechanisms by which birth mode may impact risk for obesity in childhood.

Limitations of this study include the retrospective design, relying on parental recall. To limit the recall error, the survey items were adopted from validated surveys and intake forms routinely used at doctors' offices. Nevertheless, future longitudinal research is necessary to confirm the results observed here. Further, such an approach would establish if, or when, developmental differences emerge, and whether those who exhibit developmental delays eventually catch up in development. The survey employed did not comprehensively characterize the myriad of factors that may exist during the prenatal period that could lead to the decision to have a CS birth, such as health conditions of the mother or fetus. The current study was also based on a convenience sample of families and children surrounding a university campus, it is possible that a larger and more representative sample would reveal differences in demographic and behavioral factors in early life based on mode of delivery. Additionally, the final sample size was limited by the number of CS births and matching for gestational age, leaving this study with N=104. Future longitudinal studies among larger samples of children are necessary to comprehensively understand the long-term implications of birth mode on physical and cognitive development in children. Finally, factors such as maternal existing conditions, or fetal health, development, or genetics should be examined in

future prospective studies. Future research should also compare the microbiomes of the children during development.

The aforementioned limitations notwithstanding, the strength of this study is the comprehensive questionnaire design. Groups were able to be compared on socioeconomic status, maternal BMI, maternal weight gain, birth weight, number of previous births, and early life nutrition, which helped to rule out most of the typical variables considered to contribute to developmental and weight differences in offspring.

In conclusion, these findings point to a relationship between delivery mode and key developmental milestones and obesity risk later in middle childhood. These findings also provide novel insights into the differential impact of elective CS mode of delivery compared to emergency CS. In summary, our data support the recommendation by the World Health Organization that deliberate or medically unwarranted decisions to undergo a CS should be discouraged because of the increased associations with delayed child development and subsequent disease risk.

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Abbreviations:

CS	Cesarean Section Birth
GI	Tract Gastrointestinal Tract
ASQ	Ages and Stages Questionnaire
SDQ	Strengths and Difficulties Questionnaire
%fat	Whole Body Percent Fat
BMI	Body Mass Index
DXA	Dual-energy X-ray Absorptiometry
SES	Socioeconomic Status
SAAT	Subcutaneous Abdominal Adipose Tissue
VAT	Visceral Adipose Tissue
TAAT	Total Abdominal Adipose Tissue

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Highlights:

- Vaginally-born children attain developmental milestones earlier than CS-born children
- Vaginally-born children stood, walked, and talked earlier than Emergency CS-born children stood
- Elective CS-born children were not statistically different than vaginally-born children in attainment of standing and walking. However, vaginally-born children pulled ahead and met milestones earlier for talking, self-feeding, and dressing
- Elective CS-born children had greater adiposity in preadolescence than both Vaginally-born and Emergency CS-born children; but there are no differences in preadolescent adiposity between emergency CS-born and vaginal-born children

Developmental Milestones and Mode of Delivery

Figure 1:

Bar graph depicting the ANOVA results (Bonferroni corrected) for differences between groups (vaginal birth, emergency CS, and elective CS) on the age at which developmental milestones are reached.

Differing letters indicate significant differences between groups ($p < 0.05$). The “a” indicates significant difference from “b”, but “ab” indicates no significant difference from either “a” or “b”.

Developmental Milestones Z Score and Mode of Delivery

Figure 2:

Bar graph depicting the ANOVA results (Bonferroni corrected) for differences between groups (vaginal birth, emergency CS, and elective CS) on the z Score for reaching developmental milestones.

Differing letters indicate significant differences between groups ($p < 0.05$). The “a” indicates significant difference from “b”, but “ab” indicates no significant difference from either “a” or “b”.

%Fat Mass in Preadolescence and Mode of Delivery

Figure 3:

Bar graph depicting the ANOVA results (Bonferroni corrected) for differences between groups (vaginal birth, emergency CS, and elective CS) and %Fat mass at preadolescence. Differing letters indicate significant differences between groups ($p < 0.05$). The “a” indicates significant difference from “b”, but “ab” indicates no significant difference from either “a” or “b”.

Mode of Delivery and Central Adiposity

Figure 4:

Bar graph depicting the ANOVA results (Bonferroni corrected) for differences between mode of delivery and central adiposity at preadolescence.

Differing letters indicate significant differences between groups ($p < 0.05$). The “a” indicates significant difference from “b”, but “ab” indicates no significant difference from either “a” or “b”.

TABLE 1:
PARTICIPANT DEVELOPMENTAL MILESTONES AND CHARACTERISTICS IN PREADOLESCENCE

		Vaginal Birth (n=52)	Emergency CS (n=29)	Elective CS (n=23)	All CS (n=52)	All (N=104)	Expected/Normal*
Sex, n (%)	Male	26 (50%)	17 (59%)	10 (44%)	27 (52%)	53 (51%)	
	Female	26 (50%)	12 (41%)	13 (56%)	25 (48%)	51 (49%)	
Milestone Age, months	Support Head	2.13 ± 1.30	2.06 ± 1.16	2.26 ± 1.38	2.15 ± 1.25	2.14 ± 1.27	2-4
	Roll Over	3.80 ± 1.31	3.84 ± 1.29	4.32 ± 1.86	4.05 ± 1.57	3.92 ± 1.44	4-6
*Retrospective Response	Sit Up	4.91 ± 1.24	5.18 ± 1.62	4.92 ± 1.54	5.07 ± 1.57	4.99 ± 1.41	4-9
	Stand Alone	8.83 ± 1.64	9.95 ± 2.41	9.50 ± 2.01	9.75 ± 2.23	9.29 ± 2.00	8-15
	Walk	10.86 ± 2.29	12.14 ± 2.28	11.60 ± 2.80	11.90 ± 2.51	11.38 ± 2.29	9-12
	Feed Self	10.68 ± 3.66	12.73 ± 6.13	15.95 ± 7.03	14.15 ± 6.67	12.41 ± 5.63	12-18
	Talk	10.92 ± 3.19	14.97 ± 8.01	14.52 ± 6.35	14.77 ± 7.26	12.85 ± 5.91	12-18
Gestational Age, weeks	Dress Self	23.12 ± 7.13	27.16 ± 8.17	30.13 ± 8.61	28.47 ± 8.42	25.79 ± 8.22	18-36
	Toilet-trained	26.03 ± 10.91	28.16 ± 8.92	28.36 ± 8.13	28.25 ± 8.50	27.13 ± 9.79	22-36
		38.69 ± 1.88	38.89 ± 2.08	38.43 ± 1.62	38.69 ± 1.88	38.69 ± 1.88	
Age, years		8.65 ± 0.54	8.61 ± 0.56	8.83 ± 0.82	8.70 ± 0.69	8.68 ± 0.61	
SES, n (%)	Low	26 (50%)	9 (31%)	11 (48%)	20 (39%)	46 (44%)	
	Medium	12 (23%)	8 (28%)	7 (30%)	15 (29%)	26 (25%)	
	High	14 (27%)	12 (41%)	5 (22%)	17 (33%)	32 (31%)	
At Preadolescence (ages 7-10)	Weight Status						
	Underweight	1 (2%)	3% (n=1)	0 (0%)	1 (2%)	2 (2%)	
	Healthy Weight	32 (62%)	62% (n=18)	7 (30%)	25 (48%)	57 (55%)	
	Overweight	8 (15%)	6 (21%)	7 (30%)	13 (25%)	21 (20%)	
	Obese	11 (21%)	3 (10%)	9 (39%)	12 (23%)	23 (22%)	

Data presented as Mean ± STD unless otherwise indicated

CS, Cesarean Section Birth

SES, Socioeconomic Status, determined from eligibility for school meal-assistance programs, maternal and paternal education levels, and the number of parents with full-time employment

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Weight status is categorized by BMI-for-age-percentile as indicated by the CDC: Underweight (<5th %tile), Healthy Weight (5th %tile, <85th %tile), Overweight (85th %tile, <95th %tile), Obese (≥95th %tile)

* Expected/Normal values from Centers for Disease Control (42)

TABLE 2.**PARTICIPANT CHARACTERISTICS**

	Vaginal Birth (n=52)	Emergency CS (n=29)	Elective CS (n=23)
Age, years	8.7 ± 0.5	8.6 ± 0.6	8.8 ± 0.8
Birth weight, oz	119.4 ± 20.8	122.9 ± 19.0	118.5 ± 17.0
Weight-for-gestational age, %tile	55.1 ± 32.0	60.2 ± 30.8	57.9 ± 30.0
Maternal Pre-conception BMI, kg/m ²	26.3 ± 6.1	27.3 ± 6.6	28.2 ± 8.5
Feeding Mode, %			
Exclusively Breastfed	27	21	17
Exclusively Formula-fed	21	7	13
Mixed Feeding	52	72	70
Breastfeeding Duration, months	2.4 ± 2.7	2.3 ± 2.8	2.8 ± 3.9

Data presented as Mean ± SD