Influence of Birth Weight and Gestational Age on Cognitive Performance in Primary School Children- An Observational Study

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ABSTRACT

BACKGROUND

Cognitive performance of children is influenced by various factors like birth weight, gestational age, socio economic factors, environmental factors, and nutritional status. We wanted to assess the influence of birth weight and gestational age on cognitive performance in school children.

METHODS

100 school children in the age group of 9 - 12 years were included in the study. Based on birth weight and gestational age, they were classified into three groups. Group I: Full term (>38 weeks of gestational age) and normal birth weight (> 2500 g) Group II: Full term (>38 weeks of gestational age) and low birth weight (< 2500 g) Group III: Preterm (<37 weeks of gestational age). Cognition was measured using differences between choice and simple visual and auditory reaction time (CVRT - SVRT) (CART - SART) & MMSE scores. Statistical analysis was done using SPSS Software version 20. Intergroup variations in means were assessed using one-way ANOVA and intragroup variations by using Tukey's post hoc analysis. Pearson's correlation & linear regression analysis was done to assess the relationship between birth weight and gestational age on cognitive function.

RESULTS

ANOVA with Tukey's post Hoc analysis shows significant difference in mean in CVRT-SVRT, CART-SART & MMSE across the three groups, and the difference in means is significantly higher between full term normal weight and preterm born children. (F= (2, 97)= 24.132, p= 0.000**) (F= (2, 97)= 6.395, p= 0.002*) (F (2, 97)= 26.168, p= 0.000**). Pearson's correlation matrix shows that there is significant negative correlation between birth weight and gestational age with reaction time. (r= -0.449*, r=-0.464*). Linear regression shows significant association between birth weight and gestational age with cognition. Reaction time (ms)= 0.818 – 0.041* (birth weight) – 0.013* (gestational age) (F (2, 97) = 17.285, p< 0.000) with an R^2 of 0.263.

CONCLUSIONS

Both birth weight and gestational age are significant predictors of cognition in primary school children. Amongst them, gestational age plays a crucial role.

KEY WORDS

Gestational Age, Birth Weight, Cognition, School Children, Reaction Time

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BACKGROUND

Birth weight is a powerful marker of early disadvantage. Both neonatal and infant mortality rates were high for children born at the lowest gestational age (preterm) and less birth weight.[1] Studies show relation of fetal and infant birth weight with health, development and well-being during adulthood. Studies shown reduced fetal and infant birth weights have strong association with development of non-insulin dependent Diabetes mellitus and increase risk of cardiovascular disease during adulthood.[2,3] Small size at birth is associated with a range of adverse health outcomes, including poor cognitive development. Studies shown academic performance in school children and adolescence age is largely influenced by low birth weight related cognitive disabilities, which are uncompounded by family environment, socioeconomic status and birth order.[4,5] various studies mainly focus on very low birth weight (< 1500 g) infants and cognitive disabilities.[6]

One of the causes for low birth weight is preterm births. (before 37 completed weeks of gestation) WHO reports that incidence of preterm delivery is causing around 1 million deaths annually. One of the leading causes of death in children fewer than 5 years is complications due to preterm birth who have various adverse outcomes to their term counterparts.[7] Research shown that preterm infants will have low brain volumes and prone for various neurological disabilities.[8] Studies have also shown young adults born preterm exhibits various adverse metabolic and cardiovascular sequel like reduced insulin sensitivity & hypertension[9] increased arterial stiffness.[10] Even though preterm children are prone for various disabilities like cerebral palsy, neurosensory impairments, the most common disability is neurocognitive deficits. Neurodevelopmental disability prevalence remains same in 6 and 11 years in preterm born children compared to peers.[11]

Studies show that Very preterm children of gestational weeks less than 28 weeks have significantly poorer academic performance and increased learning difficulties. Study demonstrates that early cognitive assessment provides moderate prediction of education outcome in preterm born children.[12] study done on various neurocognitive domains like planning, motor and executive functions, visuospatial function, inhibition, sensorimotor functions in preterm born children demonstrated impairment compared to peers.[13] Swedish national study done prospective study in preterm born children at 3 years and 11 years of age and assessed behavioural problems, adaptive problems, emotional problems, shows increase risk of mental health problems in preterm born children.[14] Study used cognitive workload model which demands increased cognition levels, decreased in preterm born children which is curvilinear relation with gestational age.[15] Preterm low birth weight 5-8 years children were assessed for cognitive functions including language and mathematical skills, demonstrated significant variation in preterm born children which depends mainly on environmental factors.[16] Our alternate hypothesis is there is a significant association between birth weight and gestational age with cognition in school children.

So, the following study was conducted to see the association between birth weights, gestational age on cognition in school children.

METHODS

The above study was conducted by the Department of Physiology, SDMCMS&H in Radhakrishna School, and Dharwad during July- October 2018 as a part of ICMR, STS, Govt. of India project. Approval from the Institutional Ethical Committee and Permission from the head of the school was taken before the study. Informed consent from the parents or guardian for participation of the children in the study was taken. 100 school going children, irrespective of sex, between 9 to 12 yrs. of age selected randomly from rural area residing in the residential school of Dharwad. (n=100) Sample size was decided based on previous references and time duration to complete the project. Children, who were physically handicapped, mentally retarded, had any neurological disorders, colour blindness was excluded from the study.

Study Design

Information obtained based on school health registry/ Hospital registry or information by the parents or guardian on birth weight and gestational weeks were collected. Based on birth weight children with birth weight <2500 gm were classified as low birth weight and > 2500 gm as normal birth weight. According to gestational age, children who were born before 37 weeks of gestation (<37 weeks of gestation) were classified as preterm born and who were born after 38 weeks of gestation, were classified as term born (38-40 weeks of gestation)**.** Together based on birth weight and gestational age we had three groups: Group I: Full term & Normal birth weight children (38-40 gestational weeks & >2500 g birth weight), Group II: Full term & low birth weight (38-40 gestational weeks & <2500 g birth weight), Group III: Pre term & low birth weight (< 37 weeks of gestation & <2500 g birth weight) Cognition was measured using differences between Choice and Simple Visual & Auditory reaction time (CVRT-SVRT, CART-SART) in milliseconds (ms) using reaction time apparatus (Anand Agencies, 1433/A, Shukawar Peth, Pune-411002). The visual stimulus was used to determine simple and choice visual reaction time. (SVRT & CVRT) The simple reaction involved the stimulus in the form of red light which glowed after a brief adjustable fore period (1.5 ms). On perceiving the stimulus (i.e., the red light) the subjects were instructed to press a button with right finger. The timer starts recording just after the fore period and stops when the button is pressed. The reaction time is displayed on a led screen measured in milli second (ms). Similarly, the choice visual reaction involved two stimuli one red and another green light. Either of the two light glows randomly as controlled by operator. On

perceiving the green light, the subject was asked to press the right button and if the red light was seen to glow, he is asked to press button on left. Both simple and choice Auditory Reaction Time (in millisecond) using beep tone and click were determined. Both these procedures repeated for three times and three readings which appeared on the display were noted. The least reading of the three taken as subject's best auditory reaction time and visual reaction time and recorded in the subject's proforma. Cognition was also measured using mini-mental state examination (MMSE) questionnaire. The mini-mental state examination is a test done to assess the cognitive function. It contains 11 questions which assess orientation, registration, attention and calculation, recall and language. The total score is 30. Examiner ask set of questions (given in questionnaire) to the children and based on their performance score was given.[17]

Statistical Analysis

It is an observational study done to see the association of birth weight and gestational age on cognition in school children. Statistical analysis was done by using SPSS software version 20. Values were expressed as Mean ± SD. intergroup variations were assessed using one-way ANOVA and intragroup variations by using Tukey's post hoc analysis. Pearson's correlation & linear regression analysis was done to see the relationship between birth weight and gestational age on cognitive function. P value <0.05 considered as statistically significant.

RESULTS

Table 1 shows demographical characteristics of participants. Out of 100 children 56 were boys and 44 were girls who are in the mean age of 9.8 Years (x=9.85 SD= 0.92). In order to test the hypothesis that cognition levels is influenced by gestational age and birth weight one way ANOVA is used & the results are shown in Table 2. ANOVA yielded a statistically significant difference in VRT across preterm born children, full term normal weight children & full-term low birth weight children. F= (2, 97) = 24.132, p= 0.000**. Post hoc analysis shows the difference in means is significantly higher between full term normal weight and preterm born. (p=0.00**) ANOVA yielded a statistically significant difference in ART across preterm born children, full term normal weight children & full-term low birth weight children. F= (2, 97) = 6.395, p= 0.002. Post hoc analysis shows the difference in means is significantly higher between full term normal weight and preterm born. (p=0.002**) ANOVA yielded a statistically significant difference in MMSE across preterm born children, full term normal weight children & full-term low birth weight children. F= (2, 97) = 26.168, p= 0.000**.

Post hoc analysis shows the difference in means is significantly higher between full term normal weight and preterm born.

Age of children (years)	9.8500 ± 0.92
Gender	Boys 56%, Girls 44%
Mean birth weight (kg)	2.6610 ± 0.678
Gestational age (weeks)	36.96 ± 2.411
CVRT-SVRT (ms)	0.22 ± 0.10
CART-SART (ms)	0.33 ± 0.13
MMSE Score (/30)	25.17 ± 1.27

Table 1. Descriptive Characteristics of the Participants (n=100)

Values are expressed as Mean ± SD, VRT- Visual reaction time: ART- Auditory reaction time: MMSE- Mini mental state examination: ms- millisecond

Parameter	Normal Weight Full Term (n=50)/ Group I	Low Birth Weight Full Term (n=30)/ Group II	Low Birth Weight Pre-Term (n=20)/ Group III	f Value	p Value	Post Hoc Analysis
CVRT-SVRT	.1838 ± .08033	.2163 ± .08356	.3400 ± .09947	24.132	.000**	I Vs III 0.000** II Vs III 0.000**
CART-SART	.2996 ± .15933	.3460 ± .07370	.4200 ± .10052	6.395	.002 **	I Vs III 0.002**
MMSE score	25.9200 ± .80407	24.3333 ± 1.29544	24.550 ± 1.1459	26.168	.000**	I Vs II .000** I Vs III .000**

Table 2. Cognition Parameters of Normal Weight Full Term, Low Birth Weight Full Term & Preterm Born Children (n=100)

SVRT- Simple visual reaction time: CVRT- Choice visual reaction time: SART- Simple auditory reaction time: CART- Choice auditory reaction time: MMSE- Mini mental state examination: Values are expressed as Mean ± SD. p<0.05 *considered significant.

Parameters	Birth Weight	Gestational Age	Reaction Time
Birth weight	1	r= +0.590 p=0.00**	r= -0.449 p=0.00**
Gestational age	r= +0.590 p=0.00**	1	r= -0.464 p=0.00**
Reaction Time	r= -0.449 p=0.00**	r= -0.464 p=0.00**	1

Table 3. Pearson's Correlation Matrix Shows Correlation between Birth Weight, Gestational Age and Reaction Time (n=100)

r=+ positive correlation, r= - negative correlation: p < 0.05* considered significant

Model	R	R Square	Adjusted R Square	F Change	df1	df2	Sig. F Change
1	.513[a]	.263	.248	17.285	2	97	0.00**

Table 4. Multiple Regression Analysis Shows Association of Birth Weight & Gestational Age on Cognition. (n=100)

Model	Unstandardized Coefficient B	Unstandardized Coefficient Std error	Standardized Coefficient	t	Sig
Constant	.818	.150		5.463	.000**
Birth weight	-.041	.016	-.269	-2.492	.014*
Gestational age	-.013	.005	-.306	-2.831	0.006**

Table 4a. Predictors. (Constant), Gestational Age, Birth Weight

Dependent variable: reaction time

Correlation between the variables like gestational age, birth weight and reaction time is done by Pearson's correlation as shown in Table 3. There was a positive correlation between birth weight (x= 2.6610 SD= 0.678) and gestational age (x= 36.96 SD= 2.411), r= +0.590, p= 0.00, n= 100. There was a negative correlation between birth weight (x= 2.6610 SD= 0.678) and choice- simple visual reaction time. (x= 0.22 SD= 0.10), r= -0.449, p=0.00*. There exists a negative correlation between gestational age (x= 36.96 SD= 2.411) and choice- simple visual reaction time (x= 0.22 SD= 0.10), r= -0.464, p= 0.00*. Multiple linear regressions were calculated to predict

reaction time based on their birth weight and gestational age as shown in Table 4. A significant regression equation was found. (F (2, 97) = 17.285, p<0.000) with an R^2 of 0.263. Participants predicted Reaction time (RT) measured in milliseconds (ms) is equal to RT= 0.818 – 0.041* (birth weight) – 0.013* (gestational age) Where, birth weight is measure in Kg and gestational age in weeks. Participants RT decreased 0.041 ms for each kg of body weight and 0.013 ms for each one week of gestation. Both birth weight and gestational age were significant predictors of reaction time.

DISCUSSION

Results of our study & comparison with other studies: This is an observational study done to assess influence of birth weight and gestational age on cognition. We assessed the cognition using the difference between choice and simple visual and auditory reaction time. Our study demonstrated that there is statistically significant difference exists in Reaction time across preterm born children, full term normal weight children & full-term low birth weight children. Post hoc analysis shows that both CVRT- SVRT & CART-SART is significantly higher in low birth weight children when compared to normal weight born children. Our study showed significant negative correlation between birth weight and cognition using difference between choice and simple visual reaction time. (r= -0.449, p=0.00**) which signifies that as birth weight decreases, reaction time increase which in turn signifies reduced cognition. By simple linear regression analysis, we found a significant equation to predict the reaction time using birth weight. (RT= -0.068 * Birth weight + 0.407) with R^2 value of 0.202. Our study proves the negative association between birth weight and cognition in terms of reaction time.

Results of our study is similar to work done by Strang Karlson who did multiple linear analysis adjusting for age and gender demonstrated slower reaction times in very low birth weight born young adults. (<1500 gms)[18] We have also assessed cognition in children using Mini mental state examination (MMSE) scale and shows that there exists a statistically significant difference in MMSE scores exists across three groups. Post hoc analysis shows that MMSE is significantly higher in children born with normal birth weight than those born term with low birth weight. Simple linear regression analysis demonstrates positive association between MMSE scores and birth weight with R^2 value of 0.237. Results of our study is similar to study done by Kati who studied the neuro-cognitive performance using set of tests like word recognition, clock drawing, MMSE in late adulthood who were born preterm (34-36 weeks of gestation) and results shows that MMSE score is significantly low in those who born preterm irrespective of education level.[19] Various studies also shows developmental disabilities and problem behaviours in low birth weight children during adulthood.[20]

Our study also demonstrates the effect of gestational age on cognition in children. Out of 100 children we got only 20 (n=20) who were preterm (born before 37 weeks of gestation) with low birth weight. One-way ANOVA with post hoc analysis demonstrates that both CVRT-SVRT and CART-SART were significantly higher in preterm born children when compared to full term born children. Association between gestational age and cognition were done by using Pearson's correlation and linear regression analysis. There exists a significant negative association between gestational age and reaction time (r= -0.464, p=0.00*). A significant regression equation was found RT= -0.020*(Gestational age) + 0.960 with R^2 0.216. Our study demonstrates that both birth weight and gestational age are the better predictors of cognition in children in age group of 9-12. Results of our study is similar to study done by Tatiana Izabele who assessed the impact of preterm birth with low birth weight (born with gestational age <37 weeks and birth weight < 2500 g) on neurodevelopment, cognition, and academic learning of school-age children using reaction time and other tests. They concluded the school-age subjects born prematurely and with low birth weight displayed specific brain functional alterations associated to cognitive-behavioural and learning disorders.[21] James SN showed that Association of preterm birth is more associated with ADHD-like cognitive impairments and additional subtle impairments in attention and arousal malleability using mean reaction time (MRT) and reaction time variability (RTV).[22]

Postulated mechanism: Fetal programming / Barker hypothesis suggests that Infants born premature are deprived of a critical period of intrauterine growth. From a structural point of view, premature birth may interfere particularly in the phases of glial multiplication and neuronal migration and organization, indicating the possibility of alteration in the cerebral organization. Therefore, prematurity offers the possibility of interfering in the brain maturational processes, leading to anatomical and structural interferences, which lead to functional deficits.[23]

Strengths of the Study

This study shows positive association of gestational age and birth weight with cognition in school children. Increasing birth weight might have a beneficial impact on intelligence at a population level. If a child is born preterm with low birth weight, special education services should be planned to help the at-risk group.

Limitations of the Study

As our study was done for ICMR, STS project we had to complete the project in the stipulated duration. So, we opted for small sample size, which is one of the limiting factors of the study. Impact of environmental factors like socioeconomic status, maternal education on cognition was not ruled out, so the bias might exist.

CONCLUSIONS

Low birth weight and preterm birth is associated with reduced cognition in school children of age group 9 - 12 years. Gestational age plays a crucial role compared to birth weight for cognitive performance in school children.

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