

Original Research Article

Impact of fetal malnutrition in mid-childhood and early-adolescent age

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ABSTRACT

Background: Fetal malnutrition (FM) is accompanied by short-term and long-term morbidities in children. Objective was to assess impact of FM on physical growth, blood pressure and neurodevelopment in mid childhood and early adolescent age.

Methods: An observational, retrospective, study was undertaken in an urban multispecialty hospital of Mumbai, India on a closed cohort of 54 children born in year 2006-2007. They had been assessed for their nutritional status at birth by clinical assessment of Nutrition score (CAN score) described by Metcalf. Twenty – five children had evidence of FM (FM – group) and 29 had normal nutritional status at birth (Non – FM group). They were in their mid-childhood and early-adolescent age at time of present study. Anthropometry and Blood pressure measurement of children were taken. Scholastic performance and any neurodevelopmental problem were enquired and medical records were checked.

Results: In mid-childhood and early-adolescent age, absolute risk of overweight /obesity (36% vs. 20.68%), Central obesity (8.0% vs. 3.44%), prehypertension/hypertension (8.0% vs 3.44%) and neurodevelopmental problems (24% vs. 3.44%) in FM- group children was more compared to Non - FM group. Also, FM- group children had 1.74, 2.32, 2.32 and 6.96 times more risk of overweight/obesity, central obesity, prehypertension/hypertension and neurodevelopmental problems.

Conclusions: Fetal malnutrition has significant impact on physical growth, blood pressure measurement and neurodevelopment outcome in mid childhood and early adolescent age.

Keywords: Fetal malnutrition, Growth, Development, Middle-childhood, Early adolescence

INTRODUCTION

Fetal malnutrition (FM), is defined as failure to acquire adequate amounts of fat and muscle mass during intrauterine development.¹ Nutritional and/or hormonal changes in the embryo-foetal environment exert permanent effects on a wide range of physiological processes. They influence the health and ability of an individual for lifetime, with permanent effects on growth, structure and metabolism. Alterations in fetal growth result in developmental adaptations that “programme” vulnerability to cardiovascular, metabolic, endocrine disease along with neurodevelopmental, behavioural and

intellectual disabilities.²⁻⁶ Studies on identification of fetal malnutrition at birth using clinical assessment of Nutrition score CAN score have been carried out.⁷⁻⁹ but literature on their long term follow up is scanty. This study was undertaken on a cohort of 54 children born in the year 2006-2007; who were in their mid- childhood and early-adolescence at the time of assessment. The aim was to understand the impact of fetal malnutrition (identified at birth by Clinical Assessment of Nutrition Status Score (CAN score); on physical growth, blood pressure measurement and neurodevelopment compared to those who were normal nourished at birth.

METHODS

This observational, retrospective study was conducted in paediatrics department of Bhabha Atomic research centre (BARC) Hospital Mumbai, India over a period of one year from December 2017 to November 2018.

Selection of participants

Inclusion and exclusion criteria

The study population to be included initially consisted of a cohort of 106 children born in the same hospital during the year 2006-2007. These were the full-term babies at birth whose nutritional status had been assessed by Clinical assessment of nutritional status score (CANS) method described by Metcalf.⁶ There were 36 (33.96%) new-borns diagnosed with fetal malnutrition (FM-group) and 70 (66.04%) without it (Non-FM group). The contact details of this 36 FM and gender matched 36 non-FM cohort were traced and parents were contacted telephonically in 2017. The parents being employed in the same organization; children receive health cover benefits from birth till 25 years of age. Their medical records in electronic and physical form are available. The parents were contacted telephonically and informed about the study. Some parents had been transferred, few not willing to participate or could not be contacted. This group was excluded from the study.

Parents of 54 children; (25 in FM group and 29 in non-FM group) agreed to participate and constituted the final study sample. At the time of participation, the demographic characteristic of each child was recorded, any significant illness requiring frequent hospitalization was enquired. Scholastic performance and grades were noted. In addition, presence of any diagnosed neurological /behavioural problem and information on whether child was receiving any kind of therapy was obtained. Previous health record of the child was checked and confirmed from the medical records and information on anthropometry at 2 -2.5 years & 4.5-5 years was noted.

Anthropometric measurements

Weight (Wt) was measured on an electronic digital scale to the nearest 0.1 kg and height (Ht) was measured to the nearest 0.1 cm using Stadiometer. BMI was computed using the following formula: BMI: weight (kg)/height (m).² Nutritional status was classified into underweight, normal weight, overweight and obese according to Revised IAP growth charts.¹⁰ The z-scores for three indices, i.e., weight-for-age, height-for-age, and BMI for age were calculated using IAP 2015, z- score calculator.

Waist circumference

Waist circumference (WC) was measured with an inelastic tape to the nearest 0.1 cm measuring at the end of normal expiration from the narrowest point between the lower

borders of the rib cage and the iliac crest. Age and gender specific waist circumference of ≥ 75 th WC percentile for Indian children was used to identify central obesity.¹¹

Blood pressure measurement

Systolic (SBP) and diastolic blood pressure (DBP) was measured on right arm of the child with appropriate sized cuff, in a sitting position after 10 min rest by using mercury sphygmomanometer and average of two measurements was recorded. The SBP and DBP were compared with age and gender specific percentiles of BP measurements provided in the report of the Second Task Force on blood pressure control in children.¹²

Outcome variables

Overweight and Obesity: Adult equivalent of 23 and 27 cut-off presented in age- and gender specific Revised Indian Academy of Paediatrics (IAP) growth standards.¹⁰ Central obesity: Age and gender specific waist circumference of ≥ 75 th WC percentile for Indian children.¹¹ Prehypertension and Hypertension: Blood pressure measurement between 90th to 95th percentile and above 95th percentile for age gender and height.¹² Neurodevelopmental disability: Child diagnosed with learning disability or having low Intelligence quotient (IQ) as diagnosed by Wechsler Intelligence Scale for children and/or having behavioural problems.

Statistical analysis

Statistical analysis was conducted using SPSS version 26 (SPSS Inc. Chicago, IL) statistical package. Variables with normal and non-normal distribution were presented as mean $\pm$ standard deviation and median and interquartile range. Frequencies were reported in percentage. The independent sample T test and Mann Whitney U test was used to compare continuous variables and $p < 0.05$ was considered as statistically significant. Absolute and Relative risk was calculated for overweight /obesity, prehypertension/hypertension and neurodevelopmental problems.

RESULTS

The ages of children ranged from 8-13 years (y) with no difference between the median ages (10.06 vs. 10.04y) in FM and Non-FM group.

Anthropometric parameters

At birth: At birth, children in FM- group had significantly less weight (2.65 $\pm$ 0.37 vs. 3.06 $\pm$ 0.31kg; $p < 0.0001$) and length. (49.18 $\pm$ 1.96 vs. 50.93 $\pm$ 1.54cm; $p < 0.05$) compared to Non-FM group and they continued to weigh less till 2-2.5 years of age (10.29 kg vs. 11.39kg; $p < 0.05$). Around the age of 4.5 -5 years the weight in both the groups were similar (16.75 vs. 17.07kg; $p = 0.66$).

Table 1: Anthropometric characteristics, blood pressure measurement and frequency of medical illness in children with and without fetal malnutrition (FM group & Non-FM group).

Characteristics	FM (N=25)	Non-FM- group (N=29)	P value
At birth			
Weight (kg), Mean (SD)	2.65 (0.37)	3.06 (0.31)	0.0001*
Length (cm), Mean (SD)	49.18 (1.96)	50.93 (1.54)	0.012*
Head circumference (cm), Mean (SD)	33.62 (2.30)	34.15 (1.07)	0.44
At 2-2.5 years			
Weight (kg), Mean (SD)	10.29 (1.62)	11.39 (1.59)	0.028*
At 4.5-5 years			
Weight (kg), Mean (SD)	16.75 (2.61)	17.07 (2.35)	0.66
In middle childhood and early adolescence			
Age (y), Median (IQR)	11.06 (0.04)	11.04 (2.91)	0.84
Weight (kg), Mean (SD)	38.87 (9.01)	36.75 (9.64)	0.41
Height (m), Mean (SD)	1.45 (0.10)	1.44 (0.12)	0.71
BMI (kg/m ²), Mean (SD)	18.24 (2.70)	17.34 (2.88)	0.24
Weight z score, Mean (SD)	0.406 (0.98)	0.0001 (0.803)	0.1
Height z score, Mean (SD)	0.502 (1.180)	0.136 (0.898)	0.17
BMI z score, Mean (SD)	0.278 (0.879)	0.093 (0.895)	0.131
Waist circumference (cm), Mean (SD)	69.5 (8.30)	68.68 (8.81)	0.78
SBP (mmHg), Mean (SD)	104.8 (8.43)	106.7 (7.80)	0.42
DBP (mmHg), Mean (SD)	65.78 (5.98)	65.48 (5.26)	0.85
Medical illness N (%) #	5 (20.0)	7 (29.0)	0.72

* Independent sample T test significant, # Chi square Significance test

Table 2: Middle childhood and early adolescence cumulative incidence and relative risk of overweight/obesity, central obesity, prehypertension/hypertension and neurodevelopmental problems in children with and without fetal malnutrition (FM-group & Non-FM group).

Outcome variable	Cumulative incidence		P value	Relative Risk	
	FM group (N=25), Frequency (%)	Non-FM group (N=29), Frequency (%)		Relative Risk	P value
Overweight and obesity	9 (36.0)	6 (20.68)	0.21	1.74 (0.72-4.21)	0.22
Central obesity	2 (8.0)	1 (3.44)	0.47	2.32 (0.22 - 24.09)	0.48
Prehypertension /hypertension	2 (8.0)	1 (3.44)	0.47	2.32 (0.22 - 24.09)	0.48
Neurodevelopmental disabilities	6 (24.0)	1 (3.44)	0.02*	6.96 (0.90 to 53.98)	0.06

* Independent sample T test significant

In middle childhood and early adolescent age**Overweight/ obesity & central obesity with absolute risk & relative risk**

In the age between 8-13y there was no statistical difference in anthropometric parameters i.e. mean weight (38.87 kg vs. 36.75 kg; p=0.41), height (145cm vs. 144cm; p=0.71), BMI (18.24 vs. 17.34; p=0.24), weight for age z-score (0.406 vs. 0.0001; p=0.1), height for age z-score (0.502 vs. 0.136; p=0.17), BMI for age z-score (0.278 vs. 0.093; p=0.13) and waist circumference (69.5cm vs. 68.68 cm; p=0.78) between the FM - group and Non-FM group.

However, the z-scores for weight, height & BMI and the mean waist circumference were high in the FM group. The absolute risk of overweight /obesity and central obesity in children exposed to FM (FM-group) was 36% and 8.0%

compared to 20.68% and 3.44% in Non-FM group. The relative risk for overweight/obesity and central obesity was 1.74 (0.72 to 4.21; p=0.21) and 2.32 (0.22 to 24.09; p=0.48) in the FM group compared to Non-FM group.

Blood pressure measurement with absolute & relative risk

Mean systolic (104.8 mm Hg vs. 106.7 mm Hg; p=0.420) and diastolic (65.78 mmHg vs. 65.48mm Hg; p=0.85) blood pressure measurements were similar in both the groups. The absolute risk of prehypertension /hypertension in FM group and Non-FM group was 8.0% and 3.44%. The relative risk for prehypertension /hypertension in FM group was 2.32 (0.22 to 24.09; p=0.48). Prehypertension/ hypertension was present in children who were overweight/ obese.

Neurodevelopmental disabilities with absolute & relative risk

There was significant difference in the neurodevelopmental problems between two groups. There were total 7 children (6/25 in FM-group and 1/29 in Non-FM group) already and undergoing therapy. In these children there was a high scatter and discrepancy of more than 20 points between verbal intelligent quotient (IQ) and performance intelligence quotient indicating specific learning disability. Amongst these 3 children had IQ less than 80. In addition, 2 children had social interaction problems and 1 child each had attention deficit hyperactivity disorder, stammering and nocturnal enuresis. The absolute risk of neurodevelopmental problems was 24% in FM group compared to 3.44% in Non-FM group; $p < 0.05$. The relative risk was 6.96 (0.90 to 53.98; $p = 0.06$).

DISCUSSION

We observed increased absolute risk and relative risk of overweight/obesity, central obesity, prehypertension/hypertension and neurobehavioral problems in children exposed to FM. Exposure of fetus to maternal malnutrition during early pregnancy leads to an increased risk of obesity and hypertension in the young adult age.^{13,14}

With the prevalence of obesity increasing every year, FM as one of the important risk factors for overweight and obesity in childhood and adolescent age requires serious attention. It was noted that overweight and obese children in the present study also had central obesity and prehypertension/hypertension which are the risk components for the metabolic syndrome. We observed neurobehavioral problems; learning disability, poor scholastic performance, social interaction problem, attention deficit hyperactivity disorder, stammering and nocturnal enuresis significantly more in children with FM and two thirds of them were normal-birthweight. Fetal malnutrition has a negative impact on the achievement scores in student life. FM children have lower IQ scores, require special education, or have a neurologic and intellectual disability, learning disorders, seizures, attention-deficit/hyperactivity disorder, anxiety, depression, internalizing and thought problems, poor social skills and autism spectrum disorder.^{6,15} Hill et al observed that central nervous system sequelae occurred primarily in fetal malnourished babies, whether AGA or SGA and had significantly lower IQ (verbal, performance scores) in the long term follow up.¹⁵ The increased absolute and relative risk of above problems highlight the significant impact FM has in middle childhood and early adolescent age. It is necessary to identify this condition in the neonatal age irrespective of their birth weight especially in our country with incidence of FM ranging from 19-40%.⁷⁻⁹ The neonates identified with FM should be closely monitored for growth, BMI, blood pressure and neurodevelopment in the childhood and further. The strength of above study is that the children were under the care of same hospital from birth till the study was carried

out. Hence the confounding factors like information on illness and behavioral issues could be correctly addressed. The drawback is small sample size; making it necessary to identify the significance of these problems in a large population/epidemiologic study.

CONCLUSION

Children with FM have an increased risk of overweight/obesity accompanied with associated risk factors of metabolic syndrome like prehypertension/hypertension and central obesity. They have significantly increased risk of neurodevelopmental problems in the mid-childhood and early adolescence.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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