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**Original Research Article**

# Association of early life factors with metabolic syndrome in school going adolescents of an urban south Indian population: a case control study

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## ABSTRACT

**Background:** Multiple factors are attributed for the increase in the prevalence of metabolic syndrome (MS) in adolescents. Association of early life factors like birth weight with adolescent MS is not clearly understood. Objectives were to study the association of early life factors with adolescent MS between aged 10- 15 years of Belagavi city.
**Methods:** Study design: Case control Study. Study period: January 2018 to December 2018. Study population: Adolescents of age group, 10 to 15 years from the schools of Belagavi, 400 adolescents (186-cases and controls-214) were enrolled and who were having waist circumference ≥90$^{th}$ percentile for that age and gender were subjected to the laboratory investigations to diagnose MS. Data regarding early life factors like birth weight, gestational age and breast feeding was obtained by parental interview.
**Results:** Overall prevalence as per the international diabetes federation criteria was 11% and a significant difference in the prevalence between cases and controls (15.05% vs 7.48%) (p=0.0160) was observed. Positive association was observed between initiation, exclusivity, and total duration of breast feeding with MS (OD: 3.66, 2.01, 1), indicating no protection of these factors for development of MS. Birth weight had a positive association with MS (OD=7.26).
**Conclusions:** The study showed no protective association between the initiation, exclusivity and the total duration of breastfeeding with MS. However, lower middle SES, family history of hypertension (HTN), central obesity, high BMI, high TG, and low HDL were significantly associated with increased risk of MS.

**Keywords:** MS, Early life factors, Adolescents

## INTRODUCTION

Metabolic syndrome (MS) is defined by the presence of multiple risk factors including central obesity, raised blood pressure, abnormal lipid levels, and raised blood sugar levels.[1] There is an increase in the prevalence of MS (MS) globally in children and adolescents especially in developing countries including India.[2-8] MS in childhood can lead to early onset of diabetes mellitus (DM), HTN, cardiovascular diseases (CVD).[9] Multiple risk factors are attributed for the development of MS, among them obesity is a major risk factor.[10] Early life factors like birth weight, breastfeeding and infant feeding practices are shown to be responsible for juvenile obesity with increased risk for development of MS.[11,12]

Birth weight is an important indicator of development of adolescent MS, which suggests the intrauterine environment experienced by the fetus. A strong association is reported between birth weight (low birth weight or high birth weight) and MS in the literature.[11-19] Larger population-based studies from developing countries have found that birth weight was not a risk factor in the development of MS during adolescence.[11-19]

The protective role of breast feeding for prevention of future onset of MS is studied extensively with

inconsistent results.[21-26] Hormones present in the breast milk like leptin and ghrelin regulate the appetite, growth, and weight to prevent obesity by affecting food intake and food preferences later in life.[8] Some Studies have reported that breastfeeding leads to lower risk of development of obesity, HTN, diabetes.[2-8] Many studies have observed that, the duration and exclusivity of breastfeeding in infancy have been inversely associated with future cardiometabolic risk.[9,20] There is a considerable literature on the association between breastfeeding and the components of MS in children and adolescents, but very few to study the association between breastfeeding and MS as a whole.[21-26]

It is crucial to identify this association to formulate strategies to prevent and plan interventions to minimize the risks for development of MS. Development of effective strategies and actions to control and prevent the prevalence of obesity-related chronic diseases is urgently needed in India.However there are no studies clearly defining association between MS and early life factors among children and adolescents in India. Therefore, the study was conducted with the objective to identify the association of early life factors with MS and it's prevalence in school going Indian adolescents'.

## METHODS

### *Study population*

The case control study was conducted between January 2018 to December 2018, among the adolescents of 10 to 15 years studying in the schools of Belagavi city, after obtaining the approval from the institutional ethical committee, 15 schools (List 1), were selected by stratification using the chit method. Prior to the conduct of the study, permission and consent was taken from the concerned authorities, teachers and parents. A total of 2050 adolescents were screened for MS per IDF definition.[1] The students who fulfilled the inclusion criteria and whose parents consented for the study were enrolled. Parents were interviewed for the data regarding socio demographic and family characteristics, diet history, type and duration of physical activity including number of hours of media exposure, type of media exposure in the past week and early life factors like birth weight, gestational age, total duration of breast feeding, exclusive breast-feeding duration, time of initiation of breastfeeding, which was recorded in a pre-tested and pre-designed questionnaire. Following this all the participants underwent anthropometric assessment and physical examination.

### *Inclusion criteria*

Adolescents included patients aged between 10-15 years studying in schools of Belagavi city, who consented to participate (student and parental consent), meeting the MS criteria as per IDF definition were included in study.

### *Exclusion criteria*

Absentees on the day of enrollment and adolescents with no data regarding birth weight, breast feeding history etc. were excluded.

List 1: G-Government school, P-Private school, PA-Private aided.

### *Measurements*

The anthropometry included weight for age, height for age, waist circumference, hip circumference, waist: hip ratio, BMI. The girls and boys were examined in separate rooms in the presence of a third person of the same gender. Weight was measured to the nearest of 0.1 kg on a balanced scale and was recorded on a mechanical weighing scale with an accuracy of ±50 gm. A metal column height-meter (200 cm long with 0.1 cm precision) was used for height measurement. The students stood barefooted with their hand beside straight and relaxed. The heels and buttock were in contact with the column and head in the Frankfurt plane. Waist circumference was measured by a non- stretchable tape at the midpoint between the bottom of the rib cage and above the top of the iliac crest during minimal respiration. The hip circumference was taken at the level of the anterior superior iliac spine. The hip circumference <113 cm in males and <104 cm in females was considered as normal.

*The waist:* Hip ratio calculated as waist circumference/ hip circumference and values <0.84 was considered normal for females and <0.9 was considered normal for males.[1] The BMI was calculated as the ratio of weight in kilogram to the square of height in meters and then standardized for sex and age using data from Agarwal et al growth chart for the Indian children and adolescents.[1]

*Blood pressure:* Students were made to relax for 5 minutes in sitting position and after that BP cuff was tied on the right arm midway between the acromion process and olecranon (cuff should cover 40% of the circumference of the arm). BP was checked manually with calibrated mercury sphygmomanometer, first by palpatory method then auscultatory method, average of 3 readings were taken. Blood pressure ≥ 95$^{th}$ percentile for that age and gender was included in the criteria for diagnosis of MS.

*Laboratory tests*: Adolescents with waist circumference ≥90$^{th}$ percentile for that age and gender, using Khadilkar et al waist circumference percentile charts for Indian children were subjected to the laboratory investigations namely fasting blood sugar (FBS), triglycerides and high-density lipoproteins (HDL) to diagnose MS.[27]

### *Definitions*

*Cases*: Adolescents with MS as per international diabetes foundation criteria abdominal obesity (defined as Waist

circumference ≥90th percentile according to cut off points for South Asians (≥ 90 cm in boys or ≥80 cm in girls) and presence of two of the following parameters i.e., Blood pressure≥130/85 mmHg, fasting glucose ≥100 mg/dL, triglycerides ≥ 150 mg/dL and HDL-C <40 mg/dL.[1]

*Controls:* Age and gender matched adolescents. cook et al criteria were used to diagnose MS.[28]

***Birth weight***

LBW and HBW were defined as birth weight <2500 g and ≥4000 g, respectively.

***Breastfeeding***

*Initiation of breast feeding in minutes.:* time since birth to first breastfeeding.

*Exclusive breastfeeding duration in months*: Exclusive breastfeeding" is defined as no other food or drink, not even water, except breast milk (including milk expressed or from a wet nurse) for 6 months of life, but allows the infant to receive ORS, drops and syrups (vitamins, minerals and medicines).

***Total duration of breast feeding in months***

Total duration, the baby has received the breast milk since birth to complete cessation of breast milk.

***Statistical analysis***

Was carried out by using the SPSS 20.0 software. The data was analyzed by chi square test of independence for association, the independent t test was applied to compare cases and controls with mean of numerical parameters. The multiple logistic regression was used to assess the association. Bivariate analysis of each variable was performed to know the association. The statistical significance was set at 5% level (p<0.05).

## RESULTS

Out of the total 2050 adolescents screened, 400 (186-cases and controls-214) were enrolled and analyzed. Table 1 shows the sociodemographic and general characteristics of cases and controls. Majority of the study participants were in the age group of 12.78 and 13.09 (SD 1.42 and 1.47) (in cases and controls respectively) (p=0.0338), from lower-middle class socioeconomic status and studying in the government schools. Family history of HTN was present significantly in cases compared to controls (P-0.1030). The physical activity of the adolescents in both the groups was for 30minutes /day, duration of sleep of 8hours and duration of media usage one hour per day. The overall prevalence of MS among the study population as per the IDF criteria was 11% (n=44). A statistically significant (p=0.0160) difference in the prevalence between cases 15.05% (n=28) and controls 7.48% (n=16) was observed.

It was observed that the cases had higher mean values for height, weight, waist circumference, hip circumference, BMI and also systolic and diastolic blood pressure, birth weight, initiation and total duration of breast feeding, (Table 2). However, no significant difference was observed in the mean values with regard to exclusive breast feeding, triglyceride levels and blood glucose levels.

Statistical significance was not noted between cases and controls with regard to the early life factors like birth weight, initiation, exclusive and total duration of breast feeding. Birth weight was more than 2.5 kg (p=0.6466), initiation of breast feeding was less than 30 mins (p=0.123), exclusive breast-feeding duration was between 3-6 months (p=0.900) in both cases and controls.

Bivariate analysis performed in adolescents with MS showed no significant difference between cases and controls with respect to birth weight, exclusive and total duration of breastfeeding. However, it was observed that MS was more prevalent in adolescents with birth weight more than 2,5 kg, prolonged exclusive breast-feeding duration for 7-12 months and total duration of breast feeding of 13-24 months.

Multiple regression analysis showed a significant positive association between the components of MS namely blood pressure, triglyceride levels and FBS and development of MS with odds ratio of 1, 31.69, 8.12 respectively (Table 3). This observation indicates that chance of developing MS increases with HTN, raised triglyceride and FBS levels A positive association observed between early life factors i.e., duration of exclusive and total duration of breast feeding, initiation of breast feeding, with MS with odds ratio of 3.66, 2.01, 1 respectively, indicating there was no protection with exclusive breastfeeding, breast feeding duration for development of MS. Birth weight also shows positive association with MS with odds ratio 7.26, which was statistically significant.

**Table 1: Socio demographic and general characteristics of study participants.**

| Variables | Cases, n (%) | Controls, n (%) | P value |
|---|---|---|---|
| **Socio demographic profile** | | | |
| Age (In years) (mean) | 12.78±1.4 | 13.09±1.47 | 0.0030 |
| Gender-male | 118 (63.44) | 102 (47.66) | 0.0020 |
| Lower middle-class SES (Modified B. G. Prasad classification) | 13 (46.43) | 8 (50) | 0.0700 |
| Government school | 127 (68.28) | 135 (63.08) | 0.0001 |

Continued.

| Variables | Cases, n (%) | Controls, n (%) | P value |
|---|---|---|---|
| **Parents primary education** | | | |
| Father's education | 78 (42.47) | 102 (47.66) | 0.0010 |
| Mother's education | 101 (54.30) | 99 (46.26) | 0.0010 |
| **Family history** | | | |
| HTN | 24 (12.90) | 17 (7.94) | 0.1030 |
| Diabetes | 11 (5.91) | 15 (7.01) | 0.1030 |

**Table 2: Variables of study participants.**

| Variables | Cases | | Controls | | T value | P value |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| **Anthropometry** | | | | | | |
| Height (cm) | 147.81 | 7.74 | 146.00 | 8.74 | -2.1847 | 0.0295* |
| Weight (Kg) | 46.07 | 11.20 | 39.26 | 7.64 | -7.1764 | 0.0001* |
| Waist circumference (cm) | 84.30 | 6.73 | 60.61 | 12.98 | -22.4125 | 0.0001* |
| Hip circumference (cm) | 84.16 | 13.94 | 63.81 | 16.98 | -12.9773 | 0.0001* |
| Waist: Hip ratio | 0.88 | 0.05 | 0.88 | 0.05 | 0.5509 | 0.5820 |
| BMI (Kg/m$^2$) | 20.50 | 3.26 | 18.06 | 2.35 | -8.6579 | 0.0001* |
| **Components of MS** | | | | | | |
| Waist circumference (cm) | 84.30 | 6.73 | 60.61 | 12.98 | -22.4125 | 0.0001* |
| Systolic (mmHg) | 108.62 | 11.15 | 105.89 | 7.42 | -2.9207 | 0.0037* |
| Diastolic (mmHg) | 68.28 | 6.02 | 66.56 | 6.60 | -2.7069 | 0.0071* |
| TG (mg/dl) | 117.91 | 43.66 | 111.38 | 26.93 | -1.8248 | 0.0688 |
| HDL (mg/dl) | 46.74 | 7.18 | 48.49 | 6.24 | 2.6150 | 0.0093 |
| Blood glucose (mg/dl) | 90.25 | 11.72 | 89.35 | 11.01 | -0.7927 | 0.4284 |
| **Early life factors** | | | | | | |
| Birth weight (kg) | 2.68 | 0.31 | 2.61 | 0.27 | -2.0828 | 0.0379* |
| Inter. between birth to breast milk (mins) | 42.58 | 28.70 | 53.27 | 36.58 | 3.2168 | 0.0014* |
| Exclusive breast-feeding duration (months) | 6.30 | 1.21 | 6.14 | 1.09 | -1.3586 | 0.1751 |
| Total duration of breast feeding (months) | 21.94 | 5.68 | 20.54 | 6.35 | -2.3083 | 0.0215* |

*p<0.05.

**Table 3: Multiple logistic regression analysis of status of MS by different variables.**

| Independent variables | Odds ratio | Std. errs. | Z value | P value | 95% CI for OR | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| **Exclusive breast-feeding duration (months)** | 3.66 | 3.60 | 1.3200 | 0.1860 | 0.53 | 25.08 |
| **Total duration of breast feeding (months)** | 2.01 | 1.62 | 0.8600 | 0.3880 | 0.41 | 9.77 |
| **Inter between birth to breast milk (mins)** | 1.00 | 0.01 | -0.3400 | 0.7320 | 0.97 | 1.02 |
| **Birth weight (kg)** | 7.26 | 8.01 | 1.9000 | 0.0500* | 0.83 | 63.16 |
| **SBP (Centile)** | 1.02 | 0.03 | 0.7900 | 0.4270 | 0.96 | 1.09 |
| **DBP (Centile)** | 1.12 | 0.05 | 2.4500 | 0.0140* | 1.02 | 1.22 |
| **TG (mg/dl)** | 31.69 | 25.02 | 4.3800 | 0.0001* | 6.75 | 148.90 |
| **HDL (mg/dl)** | 96.08 | 129.21 | 3.3900 | 0.0010* | 6.89 | 1340.67 |
| **Blood glucose (mg/dl)** | 8.12 | 6.73 | 2.5200 | 0.0120* | 1.60 | 41.26 |
| **BMI (Kg/m$^2$)** | 1.07 | 0.10 | 0.7800 | 0.4380 | 0.90 | 1.28 |
| **Waist circumference (cm)** | 1.01 | 0.03 | 0.1800 | 0.8590 | 0.95 | 1.07 |

## DISCUSSION

Multiple factors in early life predispose to the development of MS during adolescence. The rising prevalence of both the individual components of MS as well as complete MS indicates a need to identify these risk factors to plan the preventive strategies for at-risk populations.[29,30] The present case control study conducted among school going adolescents between 10-15 years to identify the association between early life factors and MS found no protective association.

Our study observed no protective association between MS and initiation, exclusivity and total duration of breastfeeding. Observational cross sectional studies from low and middle income countries conducted among obese adolescents, have reported similar observations.[21,24] A larger population based cross sectional study among 5258

Iranian adolescents, have also shown no evidence that longer duration of breastfeeding duration was protective against cardiovascular disease risk factors and also found no association between dose response relationship.[22] In contrast ,other studies did find a correlation between breast feeding duration and a reduced incidence of MS in later life. Cross sectional studies from China conducted among school going children between 7-17 years, have shown that breastfeeding longer than 6 months duration was inversely associated with development of MS indicating breastfeeding may reduce the risk of MS.[3,20] Similar inverse association is reported in a larger cross-sectional study among children and adolescents from Spain.[13] A Serbian case control study among obese adolescents between 10-16 years ,breast feeding was more prevalent in obese children than children with MS, indicating that lack of breastfeeding is a risk factor for development of MS.[25] Majority of the studies in a systematic review conducted by Lauren Wisnieski et.al to find the evidence for the association between breastfeeding and development of MS showed a significant association.[26] Majority of these studies showing a protective association are observational cross sectional, retrospective studies conducted among obese adolescents. However, our study compared obese vs non obese children, screened from the schools of the community using IDF criteria, indicating stronger study design.

Birth weight reflects the pattern of intrauterine growth which involves a complex interaction between parental genes and intrauterine environment. The association of birth weight and development of MS has been studied by many investigators with conflicting results .Multiple logistic analysis in our study showed that Birth weight has a significant positive association with MS (odds ratio 7.26), indicating that babies with birth weight of more than 2.5 kg were at risk of development of MS. Studies have shown that both lower birth weight and large for gestational age babies were at increased risk for having MS in adulthood.[11-19] CASPIAN study including 4811 Iranian students 6-18 years of age showed that a birth weight over 4000 gm in boys and less than 2500 gm in girls increased the risk of having MS.[23]

The overall prevalence of MS in our study was 11% with a higher prevalence in adolescents with increased abdominal obesity (cases)as against non-obese adolescents (7.48%:controls).Studies from other Asian countries have shown a higher prevalence similar to our observations.[29,30] In contrast ,many Indian studies have reported a lower prevalence of 1.5%-9.9%.[2-9] In a cross-sectional study from North India, the prevalence of MS using IDF criteria among urban adolescents was 3% and from Shimla had a prevalence of 3.3%.[5,10] Other Indian cross- sectional studies using ATP III criteria have shown a prevalence of 3.8% to 4.2%.[4,6] Higher prevalence of MS in our study when compared to the other Indian studies could be because of the difference in the definition, different study setting, and population .We also observed increase in the prevalence of MS among non-obese adolescents in the control group. Literature shows evidence of obese individuals need not be always at risk to develop MS and also reports, 40% of the normal adults of normal weight having metabolic abnormalities that are typically associated with obesity. The components of MS BMI and waist circumference, SBP, DBP were associated significantly with development of MS in the study, which are similar to other Indian studies.[6,8]

First Indian population-based case control study among adolescents to find association between early life factors and MS with adequate sample size, by using a universally accepted age-related criterion to define MS and interpreting the anthropometric measurements using the chart specific to the Indian population. This study also adds to the existing data on prevalence of MS in normal adolescents. However, data being collected from the parents retrospectively may recall bias while collecting the data and may be the limitation of the study.

## CONCLUSION

In conclusion, the present study showed no protective association between the initiation, exclusivity, the total duration of breastfeeding and MS. However, Birth weight shows positive association with MS and increase in the prevalence of MS among the study population. Our study also adds to the current knowledge that obesity per se does not imply presence of MS in the individual. Small proportion of lean individuals also harbor the changes suggestive of MS. A larger population based prospective cohort study is recommended to establish the association between early life factors and MS.

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