



Research Brief

Cardiac changes in children hospitalized with severe acute malnutrition: A prospective study at tertiary care center of northern India

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ABSTRACT

Severe acute malnutrition (SAM) may affect cardiac structure and function. Cardiac changes in sick children with SAM have received little attention in the literature. Children aged 6–60 months with SAM were cases, and age and sex matched children were controls. Cardiac biomarker levels were measured by the quantitative the Enzyme-linked immunosorbent assay (ELISA) method, and echocardiography was used to assess cardiac changes in all children. The study included 76 children in each group. Children with SAM had less left ventricular mass and increased myocardial performance index as compared with controls ($p < 0.0001$). Cardiac biomarker levels were increased in children with SAM ($p < 0.0001$). Cardiac changes and biomarker levels were comparable in children with edema and children without edema except creatine kinase-MB ($p = 0.01$).

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1. Introduction

Severe acute malnutrition (SAM) clinically manifested as marasmus and kwashiorkor; however, kwashiorkor represents most severe phenotype of edematous malnutrition.^{1,2} And it was believed that children with SAM, especially with edema were at increased risk of cardiac morbidity and sodium overload which subsequently leads to early death during treatment.^{3,4} Cardiac changes in children with SAM investigated so far reveal that there are reduced cardiac mass, and cardiac indices were in proportion to body surface area.⁵ Cardiac troponin-I (cTn-I) is a highly specific marker of cardiac injury and is not yet investigated for cardiac damage in children with SAM. The present study was carried out to determine cardiac mass, cardiac function, and biomarker profile in hospitalized children with SAM.

2. Methods

This is a prospective case control study conducted from September 2016 to May 2018 in a teaching hospital of northern India. Children aged 6–60 months fulfilling the World Health Organization criteria of SAM⁶ were cases, and age and sex matched children were included as controls. Exclusion criteria were preterm infant or intrauterine growth restriction (IUGR), inborn error of metabolism, congenital anomalies, chronic renal failure, cerebral palsy, chronic liver disease, and chromosomal abnormalities. The study was approved by the ethical committee and informed consent was obtained from the parents before the study. Variables recorded were demographic, anthropometry, history, clinical examination, and laboratory results. Cardiac biomarker levels were estimated by the Enzyme-linked immunosorbent assay (ELISA) kit as per manufactures guidelines (e methods in the [supplement](#)).

2.1. Echocardiography

Imaging was performed with the patient in a recumbent or lateral decubitus position. Left ventricular mass (LVM), left ventricular mass index (LVMI), fractional shortening (FS), ejection

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fraction (EF), and myocardial performance index (MPI) were calculated. (e methods in the [supplement](#)).

2.2. Statistical analysis

Data were analyzed by using SPSS (version 1.6). The numerical data were represented as mean. For the comparison of the two groups, the Student's *t*-test was used for parametric and the Mann–Whitney *U* test was used for nonparametric data. Multiple groups were compared using the analysis of variance test. For all tests, the difference was considered significant if the probability *p* is < 0.05.

3. Results

During the study period, 122 children with SAM were admitted, of which 12 met exclusion criteria, 2 were left against medical advice, and echocardiography could not be performed in 32 as they were admitted during 8 pm–9 am. We enrolled 76 children with SAM (49 with kwashiorkor and 27 with marasmus phenotype) and 76 healthy children. Baseline characteristics of the study population are shown in ([Table 1](#)).

3.1. Echocardiography parameters

LVM (18.29 vs 31.29 g) and LVM as indexed with body surface area (LVMI) in children with SAM (36.85 vs 42.4 g/m²) were significantly decreased in cases in comparison to control children (*p* < 0.0001). MPI in children with SAM (0.70 vs 0.43) was significantly increased in cases in comparison to control children (*p* < 0.0001). The means of EF (63.64 vs 66.1%) and FS (31.79 vs 35.94%) were normal in both groups ([Table 2](#)). LVM (18.47 vs 17.92 g), EF (64.65 vs 63.97%), MPI (0.69 vs 0.73), and FS (31.70 vs 31.64%) were comparable between children with edema and children without edema (*p* > 0.05) ([Table 2](#)).

3.2. Cardiac biomarkers

Brain natriuretic peptide (BNP) (169.3 vs 15.14 pg/ml), cTn-I (0.24 vs 0.01 ng/ml), and creatine kinase-MB (CK-MB) (29.4 vs 2.54 ng/ml) levels were significantly increased in cases in comparison to control children (*p* < 0.0001) ([Table 2](#)). The levels of cardiac biomarkers, BNP (255.13 vs 120.13 pg/ml), cTn-I (0.40 vs 0.15 ng/ml), and CK-MB (46.56 vs 19.78 ng/ml) were increased in children without edema but significant difference was observed in CK-MB (*p* = 0.01) ([Table 2](#)).

4. Discussion

Cardiac changes in malnourished children have been investigated in the prior studies showed that there is decrease in cardiac mass and impairments in ventricular functions.^{7,8} Later studies have confirmed decrease in cardiac mass but revealed difference in ventricular functions.⁵ However, these studies were on 'stable' malnourished children with different grades of undernutrition. The present study was carried out on 'sick' hospitalized children with SAM and compared with age and sex matched healthy control children.

4.1. Echocardiography parameters

In a recently published study by Brent et al,⁹ performed on sick children with SAM, the authors found significantly reduced LVM in children with SAM as compared with controls, while significantly reduced LVM was observed in children with edema when compared with children without edema. We found a similar observation that there was significant decrease in LVM in cases as compare with controls, whereas there was no difference observed in LVM between children with and children without edema. The later finding might be due to differences in severity of phenotypes of children with SAM. MPI is the measure of systolic and diastolic function of heart, and studies have reported that MPI is

Table 1
Baseline characteristics of study population.

SN	Variables		Case(n = 76)	Control (n = 76)	p value
1	Age (months)	6–12	10	14	0.15 ^e
		13–36	44	49	
		37–60	22	13	
			28.84 ± 15.19	24.47 ± 12.25	
	Age of presentation (mean ± SD)				0.05 ^f
2	Sex	Male	47	42	0.51
		Female	29	34	
3	SES ^a	Upper lower	29	26	0.004 ^g
		Lower	46	08	
4	MUAC ^b mean in cm ± SD		9.73 ± 1.3	13.43 ± 0.52	<0.0001
5	Weight mean in kg ± SD		7.06 ± 2.31	12.26 ± 2.66	<0.0001
6	Height mean in cm ± SD		72.90 ± 10.19	86.16 ± 10.05	<0.0001
5	BSA ^c mean in m ² ± SD		0.37 ± 0.06	0.57 ± 0.11	<0.0001
6	BMI ^d mean in m ² ± SD		9.63 ± 0.75	15.39 ± 1.16	<0.0001
7	Edematous malnutrition		49	Nil	
8	Non edematous malnutrition		27	Nil	
9	Pneumonia		52	Nil	
10	Acute diarrhea		54	Nil	
11	Meningitis		18	Nil	
12	B-complex deficiency		47	Nil	

^a SES: socioeconomic status.

^b MUAC: mid upper arm circumference.

^c BSA: body surface area.

^d BMI: body mass index.

^e *p* value was calculated by the chi-square test.

^f *p* value was calculated by the Mann-Whitney *U* test.

^g *p* values was calculated by the Fisher exact test.

Table 2

Comparative analysis of echocardiography parameters and cardiac biomarkers in the study population.

Variables	Case (n = 76)	Control (n = 76)	p value ⁱ	Edematous (n = 49)	Non-Edematous (n = 27)	p value
Echocardiography parameters (mean ± SD)						
LVM ^a (g)	18.29 ± 3.33	31.29 ± 6.81	<0.0001	18.47 ± 3.43	17.92 ± 3.12	0.48
LVMi ^b (g/m ²)	36.85 ± 13.49	42.40 ± 8.48	<0.0001	35.43 ± 11.85	39.04 ± 15.98	0.30
EF ^c (%)	63.64 ± 2.80	66.10 ± 1.41	<0.0001	64.65 ± 2.82	63.97 ± 2.75	0.31
FS ^d (%)	31.79 ± 3.79	35.94 ± 1.78	<0.0001	31.70 ± 3.91	31.64 ± 3.91	0.94
MPI ^e	0.70 ± 0.10	0.43 ± 0.035	<0.0001	0.72 ± 0.11	0.68 ± 0.09	0.07
Cardiac biomarker (mean ± SD)						
BNP ^f (pg/ml)	169.30 ± 256.56	15.14 ± 7.17	<0.0001	120.13 ± 205.2	255.13 ± 313.6	0.05
cTn-I ^g (ng/ml)	0.246 ± 0.61	0.010 ± 0.00	<0.0001	0.15 ± 0.47	0.40 ± 0.67	0.09
CK-MB ^h (ng/ml)	29.41 ± 41.61	2.54 ± 2.77	<0.0001	19.78 ± 30.52	46.56 ± 52.19	0.01

^a LVM: left ventricular mass.^b -LVMi: left ventricular mass index with body surface area.^c EF: ejection fraction.^d FS: fractional shortening.^e MPI: myocardial performance index.^f BNP: brain natriuretic peptide^g cTn-I: cardiac troponin-I.^h CK-MB: creatine kinase-MB.ⁱ p value was calculated by the Mann–Whitney U test.

reproducible and independent of arterial pressure, heart rate, after load, and preload in patients who are in a supine position.¹⁰ MPI increases in cardiac dysfunction. In the present study we observed increased MPI in children with SAM as compared with controls, while means of EF and FS was in the normal range. Similar results were reported by El Razaky et al¹¹ and Meena et al¹² MPI was increased in both children with edema and without edema, but the difference was not significant. MPI was an early marker of ventricular dysfunction in children with SAM while FS and EF were normal.

4.2. Cardiac biomarkers

These are routinely used to assess cardiac function (BNP) and myocardial injury (troponin and CK-MB). cTn-I is a highly specific marker of cardiac injury, and it is better than CK-MB. El-Sayed et al⁵ reported that cardiac proteins are increased in children with SAM or complicated SAM. We also observed that cardiac biomarker levels (BNP, cTn-I, and CK-MB) were significantly increased in children with SAM when compared with controls, similar results were reported by Abu Faddan et al¹³ and Brent et al⁹. Increased levels of BNP suggested that ventricular dysfunction in children with SAM and myocardial injury was evident by increased levels of cTn-I and CK-MB. Cardiac biomarker levels were increased in both children with edema and without edema; however, these levels are more increased in children without edema, similar results were reported by Abu Faddan et al¹³ Prior evidence showed that children with edema were more vulnerable for cardiac dysfunction,^{3,4} but we observed that comparable functional parameters between children with edema and children without edema while more increased cardiac biomarker levels were seen in children without edema. This observation might be due to the fact that pathogenesis of edema in children with SAM is not because of cardiac origin but clinical and biochemical complications and comorbidities may predispose these children for cardiac dysfunction. A similar observation was reported by El-Sayed et al⁵ and Abu faddan et al¹³ and they concluded that cardiac troponin-T was significantly increased in malnourished children with anemia, sepsis, and electrolyte deficiency. The limitation of the present study was that, we did not investigate the effect of clinical and biochemical complications and comorbidities, in sick children with SAM, and we did not assess cardiac function after nutritional recovery. There is need

for further studies with disease-matched control children to assess the effect of complications and comorbidities on cardiac functions in children with SAM.

5. Key message

Cardiac mass is reduced, and ventricular dysfunction and myocardial injury are earliest detected by MPI, BNP and cTn-I, respectively, in children with SAM.

Declaration of competing interest

All authors have none to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ihj.2020.01.005>.

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