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Correspondance

Early marker of left ventricular dysfunction in echocardiography and cardiac biomarkers in sick children with severe acute malnutrition

We would like to thank Takia et al for their great interest in our published article entitled, "Cardiac changes in children hospitalized with severe acute malnutrition: A prospective study at tertiary care center of Northern India". We agree and appreciate the remark of representation of data, it would be better to present in median (IQR) instead of mean (SD). Cardiac failure can manifest with or without normal left ventricular ejection fraction (EF), and advancement in cardiac ultrasound enable clinician to diagnose cardiac failure with normal EF. Myocardial performance index (MPI)[1,2], and Global longitudinal strain (GLS)[3] would identify global cardiac dysfunction with preserved EF and FS. There are limited studies which correlate MPI and GLS in sick children with severe acute malnutrition (SAM). We attempted here to describe EF, FS and MPI in sick children with SAM and have different opinion in response to statement of "conflicting correlation between MPI with malnutrition", as there is statistically significant difference observed between cases and controls in value of MPI (0.57 ± 0.13 vs 0.40 ± 0.08, $p = 0.001$) in study by El Razaky et al.[4] In our study we observed that mean (SD) values of EF, fractional shortening (FS) were in normal range, while myocardial performance index (MPI) was abnormal in all children. Similar results were reported by Meena et al,[5] Bebars et al[6] and Akdeniz et al,[7] whereas the median (IQR) values of MPI in normal range, but individual analysis of MPI reveals that 26/88 (29.5%) of children showed abnormal values in a study by Brent et al.[8] This variability in results might be due to difference in severity of phenotypes of SAM and different grade of severity of electrolyte imbalance or trace element deficiency which affect cardiac functions. We already mentioned in our article that MPI is reproducible and independent of arterial pressure, heart rate, after load, and preload in patients who are in a supine position and it did not require indexing with body surface area. Myocardial performance index (MPI) can be calculated by Tissue Doppler (TDI-MPI), Pulse wave Doppler (PWD-MPI) and M-mode and its normal range depend on method of calculation, and we follow similar range as used by Brent et al.[8] We accord with Takia et al that the time intervals (systolic and diastolic) would be measured in different cardiac cycle by PWD-MPI, as these time intervals are simultaneously measured in a single cardiac cycle in TDI-MPI. To avoid beet-to-beat variation we measured MPI on several occasions and took average of three consecutive readings.[1,8] Myocardial fiber deformation (strain) is assessed by Global longitudinal strain (GLS) using 2D speckle tracking echocardiography (2DSTE). We consent with suggestion of Takia et al that Global longitudinal strain (GLS) is better index of myocardial dysfunction than left ventricular ejection fraction and able to identify subclinical myocardial dysfunction, when other echocardiography parameters are normal or with inconsistent results.[3] Age, sex, end diastolic volume may affect the normal value of GLS,[3] as El Razaky et al[4] showed that children with moderate malnutrition have 42.1% variation in values of GLS is because of body mass index. Hence, whether it is precise to compare the values of GLS in children with severe acute malnutrition (SAM) to the normal range of GLS in healthy children? It requires further study to establish it and indexing of GLS values with length or body surface area yet to establish?

In our study we estimated B-type natriuretic peptide (BNP), cardiac troponin-I (cTn-I) and creatine kinase-MB (CK-MB). Among these cardiac biomarkers, BNP has established role to recognize ventricular dysfunction irrespective of etiology[9] and cTn-I is considered as gold standard to detect myocardial injury irrespective of etiology.[10] In our study we mentioned that cardiac biomarker like cardiac troponin and BNP[11] would increase in children with SAM. We found that , out of 86 children with SAM, 32 (37.2%) children were increased BNP levels and 46 (53.5%) children had increased cTn-I levels. Median (IQR) values of BNP (pg/ml) and cTn-I (ng/ml) were 213 (111, 590) and 0.16 (0.10, 0.33) respectively. Prior work of literature suggested that increased values of cTn-I[12] and BNP[13] were correlated with presence of sepsis or sepsis induced myocardial dysfunction. We agree as it is expected to have higher value or may have its low specificity in comparison to SAM children and children with SAM with presence of sepsis, pneumonia and diarrhea. It would be better to opine that the values of BNP and cTn-I levels would further increase in children with SAM, presenting with features of cardiac failure or septic shock.[10,14]

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Author contribution

Dr. Sunil Kumar Rao: Concept, Design, Drafting of the manuscript, Critical analysis.
Dr. Dharmendra Jain: Concept, Drafting of manuscript.
Dr Tej Bali Singh: Concept, interpretation and statistical analysis.

Declaration of Competing interest

No Conflicts of interest.

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Reply in response to comments not to be published in letter to editor

We would ready to make correction, here we mentioned point by point explanation, and these are as follows.

Table-1

(i) "e" Comparison of more than two categorical variables should be through
ANOVA, however author has wrongly written it as chi square test
ANOVA is used in case of numerical variables to compare the mean (SD) etc, here number of subjects lies in the different age groups between two study groups are presented so X^2- test is used.

(ii) "f" Comparison of continuous variable with means should be through student t test, for Mann-Whitney U test, medians should be used.
Age of presentation is mentioned here in form of mean (SD), but here SD is more than half of the mean i.e. it is not follow the Gaussian distribution, so to test the significance difference between the mean values Mann-Whitney-U-test is used. Alternatively median (IQR) may be presented in the table, accordingly, comparison of two median, can be used.

(iii) "g" Chi square test should be used rather than fisher exact test
Yes, here cell frequencies (expected) is more than 5 so, X^2-test should be used instead of Fisher's exact test. But approximately both tests in this situation give nearly same results i.e. significant difference exists ($p<0.05$).

Table-2

(i) Mann –Whitney U test is used for p value, we feel median values should be used, rather than mean values
The Mann-Whitney U test is applicable in variables that are not following Gaussian distribution, moreover median or mean rank would required to compare variables, it will be decided by shape of distribution of data. If shape is identical then median will be the choice or if shape is different than mean ranks will be the choice[1].

We would like to delete superscript i from p value in Table-2, by mistake it was mentioned.

(i) Echocardiography parameters mean (SD) presented in Table-2 are following Gaussian distribution, therefore, student "T" test is used to compare the mean values between two groups.

(ii) Cardiac biomarkers, here SD is higher than half of mean so does not follow the Gaussian distribution. Therefore parameters should be presented in Median (IQR), and Mann-Whitney –U-test is used to compare the median values.

Reference

1. Mann-Whitney U test using SPSS statistics. Available at https://statistics.laerd.com/spss-tutorials./mann-whitney-u-test-using-spss-statistics.php. Assessed on 4 may 2020.